

# CONTROL OF TOBACCO-RELATED CANCERS AND OTHER DISEASES

PROCEEDINGS OF AN INTERNATIONAL SYMPOSIUM  
January 15-19, 1990, TIFR, Bombay

*Edited by*  
Prakash C. Gupta  
James E. Hamner, III  
P. R. Murti



# Control of Tobacco-related Cancers and Other Diseases

Proceedings of an International Symposium

Prakash C. Gupta,  
James E. Hamner, III  
and P. R. Murti

Tobacco use is widely recognized as the most important preventable cause of death and disease in the world today. In most countries its use is synonymous with cigarette smoking, but in others tobacco is used more often in other forms as well. In India, tobacco is more commonly used in the form of *bidi* smoking and betel quid (*pan*) chewing, even more than in cigarettes.

The health consequences of cigarette smoking and other forms of tobacco use encompass a wide spectrum of diseases including cancers of the mouth, lung, larynx, pharynx and oesophagus; diseases of the heart, circulatory system and lungs; and if used during pregnancy, adverse effects on the fetus. Even second-hand passive smoking is shown to cause and influence the risks for other diseases.

Tobacco control in any country, however, is not simply a health problem. It has major implications for economics, agriculture, law, and individual and social behaviour. Therefore, tobacco control must involve a multidimensional, multidisciplinary approach.

In this volume, the issue of tobacco control is addressed from many points of view by leading international experts in clinical medicine, public health, biostatistics, experimental and behavioral sciences, agriculture, law and policy analysis. The articles provide an in-depth overview on various topics central to the theme of tobacco control. They describe different ways in which tobacco is used, their adverse health consequences with special emphasis on oral health and cancer, evidence from experimental studies, experiences with tobacco control and intervention programmes, and specific legal and policy issues.

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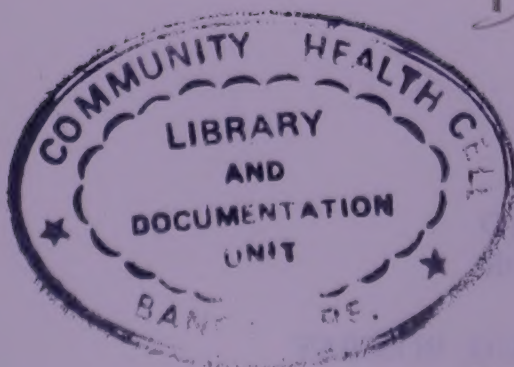
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We convey our deep sense of appreciation to Dr Fali S. Mehta, Head, Basic Dental Research Unit, Tata Institute of Fundamental Research, for his support and guidance; to our colleagues in the Basic Dental Research Unit, particularly Dr R. B. Bhonsle and Dr D. K. Daftary; and to our friends in the Tata Institute of Fundamental Research for their help in organizing the Symposium, in assisting in all aspects of the Symposium, and in preparing this volume.

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The invaluable editorial assistance in preparing this volume provided by Ms Elisabeth Heseltine is deeply appreciated. Lastly, we wish to thank our excellent secretaries, Ms Charlotte Salvaggio and Mr M. C. Kuriakose for the outstanding job they did on typing the many drafts of the revised manuscripts.

Prakash C. Gupta  
James E. Hamner, III  
P. R. Murti



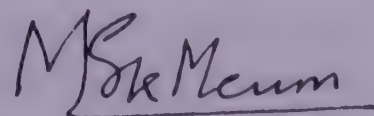
# FOREWORD

I was happy to be invited to inaugurate this International Symposium on the Control of Tobacco-related Cancers and Other Diseases, which is being held at the Tata Institute of Fundamental Research (TIFR), Bombay, during January 15-19, 1990. I looked forward to being present and to delivering personally the inaugural address; but, owing to other important official commitments, this was not possible. Tobacco-related research started in the TIFR when I was the Director, and it had my fullest support. At that time I thought of it as a short-term project; but, as often happens in scientific research, a good piece of work leads to another, and so this research is still continuing at TIFR. I am very pleased to see how valuable this work has been, constituting a very large, long-term, epidemiological study, with follow-up.

According to WHO, the use of tobacco in various forms is the largest single preventable cause of death and disease today in the world. Tobacco-related cancers, and other diseases, are among the most serious global health problems, and they are of special significance in India, since India is one of the world's largest producers and consumers of tobacco.

I am glad that the participants at this Symposium will be discussing the health problems arising from the use of tobacco from a multi-disciplinary angle. The disciplines represented include clinical and other experimental sciences, behavioural science, epidemiology, public health, law and economics. I hope you will have very fruitful deliberations and exchanges of ideas. The results and recommendations arising out of the discussions of such a distinguished group of experts will surely be most valuable and will be given the most serious consideration by all those who are responsible for improving the health and welfare of the people, particularly in the Government of India.

I wish the Symposium every success.



M. G. K. MENON

*Minister of State  
Science & Technology, Atomic Energy,  
Space, Electronics & Ocean Development  
Government of India*





# INTRODUCTION

Tobacco was introduced to the modern world in the 15th century, and into India sometime in the late 16th or early 17th century. Since then, its use has spread alarmingly fast, both within India and elsewhere; today, there is no country where tobacco is not used.

In most parts of the world, cigarette smoking is the most popular form of tobacco use. The harmful health effects of this habit have been well-recognized over the last four decades. The first major government report on the problem was the *US Surgeon-General's Report* in 1964. Subsequently, numerous studies from all over the world confirmed the deleterious role of cigarette smoking and other forms of tobacco use and augmented knowledge about the numerous adverse health consequences.

Tobacco is smoked and chewed in various forms. In India, the most common form in which tobacco is smoked is the *bidi*, and the most common form for chewing is as an ingredient of *pan* (betel quid). The relationship between betel-quid chewing in India and oral cancer was recognized during the early part of the 20th century, and several studies have confirmed the associations between various forms of tobacco use and oral cancer, precancer, and other diseases in India.

The overall health consequences of tobacco use are enormous. According to WHO estimates, 2.5-3 million deaths per year can be attributed to tobacco use. Estimates for India are around 630 000 deaths, and for the USA, close to 300 000.

In India, most of the work in this field has come from the Basic Dental Research Unit of the Tata Institute of Fundamental Research (TIFR), which is the WHO Collaborating Centre for Oral Cancer Prevention. This research began in 1966 in collaboration with the National Institutes of Health (NIH), USA, the Department of Oral Pathology, Royal Dental College Copenhagen, and the Dental Department, Rigshospitalet, Copenhagen, Denmark; this work is continuing. In these studies, over 200 000 villagers have been interviewed and examined in house-to-house surveys, and 66 000 have been followed-up annually for up to 10 years. In one of these studies, 36 000 tobacco users were educated over a period of 10 years to stop their tobacco use; the results were highly encouraging.

Tobacco is not, however, simply a health problem. Its economic impact is equally important, particularly in the USA and India, two of the largest producers of tobacco in the world. Tobacco is significant in agriculture and industry, provides revenue to the exchequer, and prompts specific questions about law and public policy. Formulation of strategies for controlling tobacco-related cancers and other diseases, therefore, requires a multidimensional approach.

The concept of hosting an international Symposium with a view to exchanging the latest scientific information for formulating tobacco control policies was a natural outgrowth of the research at the TIFR. The idea crystallized after Dr Prakash C. Gupta spent a year as a Takemi Fellow at the Harvard School of Public Health and had discussions with Professors Lincoln Chen and Michael Reich. With encouragement from Dr Fali S. Mehta, Chief of the Basic Dental Research Unit at the TIFR, and in consultation with Dr James E. Hamner, III, the NIH Project Officer, Dr Gupta requested a conference grant through the US-India Scientific Agreement, the same source through which the research at TIFR is now funded. The application was tentatively approved by Ms Linda

Vogel, Deputy Director of the US Public Health Service's Office of International Health in 1987 on an exchange visit to India to meet with Indian Government officials. On his visits to the USA, Dr Mehta met with Ms Vogel, Surgeon-General C. Everett Koop, and Dr Morris Jones of the NIH Fogarty International Center, along with Dr Hamner, in regard to the final funding, which was achieved in March 1989. During Dr Gupta's visit to the University of Tennessee, Memphis, in July 1989, Dr Hamner and he finalized the programme and planned events associated with the Symposium.

The Symposium was held during January 15-19, 1990 at the Tata Institute of Fundamental Research. A total of 46 research scientists from seven countries (Denmark, France, India, Japan, Sri Lanka, the United Kingdom and the USA) representing 30 distinguished institutions and disciplines, including biostatistics, behavioural sciences, epidemiology, clinical and experimental medicine, law, public health and public policy, participated in the Symposium. We are most appreciative of their participation and contributions. This volume contains the papers presented at the Symposium and the Consensus Summary and Recommendations arising out of it. The Consensus Summary and Recommendations were submitted to the Government of India at the end of January 1990 and were widely distributed.



## **KEYNOTE ADDRESS**





## Tobacco or health: a smoke-free society by the year 2000

ROBERT E. WINDOM

*Former Assistant Secretary for Health, US Department of Health and Human Services*

I am honoured and pleased to be a participant in this important International Symposium on Smoking and Health, being conducted under the auspices of the Tata Institute of Fundamental Research. I derive special pleasure from the fact that these scientific sessions mark a significant milestone in the long-standing partnership between India and the USA on behalf of public health.

Fifteen years ago, our forces were joined under the aegis of the World Health Organization in the conquest of smallpox, one of mankind's oldest and deadliest scourges. Here in India, you marshalled what may well have been the largest force ever assembled for a humanitarian purpose — hundreds of thousands of workers campaigning from village-to-village and house-to-house, first to contain and then to eradicate this ancient enemy. The world's last case of naturally occurring smallpox was identified in East Africa in 1977. But it was here in India, and in neighbouring Bangladesh, that ultimate victory over smallpox was assured. Your country played a pivotal role in one of humankind's greatest achievements. Now, India and the USA are joined with more than 160 other nations, members of WHO, in the quest of 'Health for All by the Year 2000'. The topic before this Symposium must be ranked among the very highest priorities if this bold goal is to be approached and eventually achieved. For there is no doubt whatever that, despite significant progress, tobacco usage remains the single greatest cause of unnecessary, preventable

mortality and morbidity in the USA and other countries in the so-called developed world. Tragically, there is every reason to believe that it is rapidly becoming the single greatest cause of needless death and disability in the developing world as well.

Let me quickly document the truth of this statement with a few figures which, though well known to most of you, are not yet widely enough accepted in the world at large. The numbers refer to the USA, but the facts apply universally:

Lung cancer, the leading cause of cancer mortality, accounts for one of every four cancer deaths in the USA, and cigarette smoking is responsible for 9 out of every 10 of these deaths. Tobacco usage is also causally related to cancer of the larynx, oral cavity and oesophagus and is a risk factor in cancers of the pancreas, kidney and bladder. Thus, it is directly related to 30% of all cancer deaths.

Cigarette smokers have 70% greater mortality from coronary artery disease than non-smokers. Smoking is thus a major independent risk factor for coronary heart disease, just as hypertension and hypercholesterolaemia are. Cigarette smoking is the major cause of chronic obstructive lung disease, particularly chronic bronchitis and emphysema, and morbidity and mortality from these causes are rising rapidly. Maternal smoking during pregnancy increases the risk of premature birth, spontaneous abortion, stillbirth and low birth-weight.



In October 1988, the worldwide problem was presented to the WHO Executive Board in these terms: 2-2.5 million premature deaths per year in the world are due to tobacco smoking. These include one-third of all deaths from cancer, 75% of those from chronic bronchitis and emphysema and 25% of those from coronary heart disease. Tobacco smoking is dangerous not only to the smokers but to nonsmokers as well, particularly children, through the damaging effects of enforced, passive smoking. The health hazards of tobacco chewing, snuff dipping and other smokeless forms of tobacco have been reappraised. These are as dangerous as smoking in terms of nicotine addiction and of oral cancer, and smoking can be as addictive as alcohol or heroin.

In response to this report and the recommendations of the Executive Board, the World Health Assembly, in May of last year, approved the plan of action for a programme entitled 'Tobacco or Health' for the period 1988-95. Thus, WHO will be actively engaged, with a strengthened programme, in the worldwide struggle against the consequences of tobacco usage.

It is most appropriate that WHO should once again assume leadership. What we know about the health consequences of tobacco usage is supported by more than 50 000 scientific studies from around the world, conducted over the past 30 years. Each year, another 2000 research findings are identified and catalogued. The scientific consensus is thus overwhelming. It is truly a problem on a global scale.

Scientists in India, and specifically at the Tata Institute of Fundamental Research, have been important contributors to the world's store of knowledge about tobacco. Pioneering work on the relationship between smokeless tobacco use and oral cancer was begun more than 20 years ago by Dr Fali Mehta, Professor Jens Pindborg, Dr James Hamner and their

associates. It is especially noteworthy that this research was initiated in the field of occupational health, a clear indication that you were years ahead of your time. You are also to be highly commended for the scope and sophistication of your intervention programmes. Few, if any, such studies can match the number of participants, the length of time they have been carefully studied, or the diversity of your intervention approaches. We in the US Public Health Service are proud that the National Institutes of Health has been a partner with you in this endeavour.

In connection with your work on smokeless tobacco and oral cancer, it is relevant to note that smokeless tobacco is receiving increased and belated attention in the USA. Medical reports and reviews by several organizations, including an Advisory Committee to the Surgeon-General in 1989, have further documented that smokeless tobacco is not a safe alternative to smoking, that such products cause oral cancer and other oral diseases, and that smokeless tobacco products are addictive. These facts, though not new discoveries, have taken on added significance for us. Consumption of smokeless tobacco increased sharply between 1970 and 1985 in the USA at a time when other uses of tobacco were declining. During that 15-year period, production of snuff increased by 56% and that of chewing tobacco by 36%. Still more alarming, surveys showed that significant increases were occurring in the use of smokeless tobacco products by young adult and adolescent males, among whom it appeared to be gaining increased popularity and social acceptance. As a consequence, the US medical, dental and scientific communities have given increased attention to smokeless tobacco, and the US Congress has become actively concerned. I am pleased to be able to report that since 1985 in my country, production of smokeless tobacco products, including all categories, has begun to decline. But this problem will clearly require continuing vigilance.



It was 26 years ago in January that the US Public Health Service issued the document *Smoking and Health: Report of the Advisory Committee to the Surgeon-General*. Its release was a major news event, occupying the front pages of the newspapers for many weeks. The Advisory Committee's conclusion was that cigarette smoking is a health hazard of sufficient importance in the USA to warrant appropriate remedial action. These words seem rather bland today; the nature of the appropriate remedial action was not specified. In the light of what we have learnt in the succeeding quarter-century, it is hard to comprehend the enormous excitement and controversy generated by that first report. It is even more difficult to comprehend how the subject can remain controversial today. The answer, of course, is that powerful and subtle forces have done everything possible to keep it controversial — to cast shadows of doubt on the most compelling scientific findings. These forces are, of course, centred in the tobacco industry, which, in a single recent year, spent US\$ 2.1 billion for advertising and promotion of tobacco usage. Subjected to such a barrage, it is not surprising that the US public continues to use tobacco, despite almost universal recognition of its hazards. There is another important reason for the persistence of this deadly habit. In 1988, the 20th *Report of the Surgeon-General on the Health Consequences of Tobacco* substantiated beyond doubt that tobacco is an addictive substance and that nicotine is the drug in tobacco that causes addiction.

The subject of addiction has been approached with great scientific care. The 1964 report referred to tobacco use as habituating; the 1979 report called smoking the prototypical substance-abuse dependency; by 1988, further research had made it clear that we no longer needed to pull our punches. To quote that report: "The pharmacologic and behavioural processes that determine tobacco addiction are similar to those that determine addiction to drugs such as heroin and

cocaine.": frank recognition of the fact of addiction has very important implications. Nicotine is a psychoactive drug. Its actions reinforce tobacco usage. Therefore, our efforts for prevention and control must address all factors — social, psychological and pharmacological. The message for health professionals is loud and clear: tobacco use is a disorder which can be remedied through medical attention. It should be approached by health care providers with knowledge, understanding and, above all, persistence, just as other substance-abuse disorders are approached. Every health care provider has an obligation to use all available opportunities to encourage smokers to quit, to assist them in the process, and to help former smokers maintain abstinence.

Moreover, the issue of addiction imposes additional obligations with respect to children and youth. We must ensure that every child, in every school and community, is educated as to both the health risks and the addictive nature of tobacco usage. This is a task for health professionals, for educators, for parents and other role models — in short, for society as a whole. In his address to the 13th World Conference on Health Education, held in the USA in 1988, the Director-General of WHO, Dr Hiroshi Nakajima, stated: "Society must make it possible for people to live healthy lives. A grand alliance of people, policy-makers, and professionals is necessary."

Dr Nakajima was referring to the entire range of problems related to disease prevention and health promotion — problems of the environment, of health-related behaviour among individuals, families and communities. But it seems to me that his clarion call for a *grand alliance* has very special application to the problem addressed by this Symposium on 'The Health Consequences of Tobacco Usage'. Nothing less than such a *grand alliance* will do the job.

Looking back over the quarter-century since the publication of the first Surgeon-General's Report, it seems to me that we in the



USA have in fact approached the formation of such an alliance. Perhaps you will pardon my pride if I take you on a brief retrospective journey, recounting a few of the highlights of our 25 years of progress.

It seems appropriate that I should do so because, in some ways, I perceive India to be at the stage we were 25 years ago. Specific problems differ, of course, as our own countries differ. But in the crucially important area of social perceptions of tobacco use, you appear to be at a point we have only recently passed. It is in this area of social acceptability that we have found our *grand alliance* most useful.

Our story is far from perfect. We still have a long way to go. But it is, I think, a success story, and I hope it may prove instructive for other countries that address the issue in their own separate contexts and circumstances. I have already made reference to the enormous news interest generated by the release of the Advisory Committee Report in 1964. This was not a one-day sensation but a sustained expression of intense public hunger for information. This hunger was fed by claims and counter-claims from many sources — both reliable and highly unreliable.

In that same year, 1964, the US Public Health Service established a small unit, almost microscopic in the vastness of the Federal Government, called the National Clearinghouse for Smoking and Health. The Clearinghouse and its successor organization, the Office on Smoking and Health, have compiled a record of accomplishment far greater than the size of their budget and staff. They have catalogued and made available to scientists, health professionals and the public an ever-growing number of research studies. They have published 21 annual reports addressing specific aspects of the tobacco problem. They have formed an enduring partnership with the major professional and voluntary associations in the private sector for the education of both health professionals and the public.

The nation's legislators have played a vital role. As early as 1965, the US Congress adopted the Federal Cigarette Labelling and Advertising Act. This law and the Public Health Cigarette Smoking Act of 1969 combined to require health warnings on cigarette packages and to ban cigarette advertising in the broadcast media. They also required the publication of the series of annual reports previously mentioned, which, in addition to their intrinsic value, provide an occasion each year for a *news event* proclaiming the hazards of smoking. Legislation in 1984 greatly strengthened the severity of required warnings on cigarette packages and advertising.

But the action is by no means confined to the federal level of government. Each year, more and more state laws and local ordinances are being enacted which restrict or prohibit smoking in public places, in the workplace, in schools and elsewhere. As of mid-1988, more than 320 local communities had such restrictions, and the number is growing rapidly.

Educators have introduced anti-tobacco curricula, some of which have been rigorously evaluated and proven effective, in many of the nation's 16 000 local school districts. With regard to economic incentives to discourage tobacco usage, tobacco products are being taxed more heavily at all levels of government, and insurance premium differentials for smokers *versus* nonsmokers are increasingly available.

What about results? Do we have some concrete evidence of progress as a result of 25 years' activity by our modest *grand alliance*? Happily, the answer is 'Yes'. Let me enumerate some of the promising findings:

Between 1965 and 1987, the prevalence of cigarette smoking among men 20 years of age and older decreased from 50% to 32%; among women, smoking prevalence declined from 32% to 27%. Putting these figures together, the prevalence of smoking among adults in the USA decreased from 40% in 1965 to 29% in



1987. Nearly half of all living adults who ever smoked have quit; there are more than 30 million ex-smokers in the US population. Between 1964 and 1985, approximately three-quarters of a million smoking-related deaths were avoided or postponed as a result of a decision either to quit smoking or not to start. Each of these avoided or postponed deaths represents an average gain in life expectancy of two decades.

While over 50 million Americans continue to smoke, more than 90 million would be smoking today if it were not for the changes in knowledge and attitudes towards smoking that have occurred since 1964. Furthermore, it is important that 90% of all adults who smoke know that it is hazardous for them to do so, and 90% say that they would quit if they were able to. Nearly two-thirds say that they have seriously tried to quit and failed — strong testimony to the addictive nature of tobacco usage. Most of them will try again, however, and many will ultimately succeed. On the basis of current trends, an additional 2.1 million smoking-related deaths will be avoided or postponed between 1986 and the year 2000.

All of these indicators of success are gratifying to those of us who have been engaged in this long campaign on behalf of public health. They are the product of rapidly expanding scientific knowledge and increasingly effective communication. Each indicator is laden with significance in human terms: every percentage point of decline in the prevalence of smoking adds literally thousands of years of productive life to our population. But perhaps most important of all, they manifest a remarkable change in the way tobacco usage is perceived by our society. It is this change that allows us and in fact encourages us to believe in a smoke-free society in the USA in the 21st century. In my view, this is the change towards which India should bend every effort.

Back in the 1940s and 1950s, cigarette smoking was the accepted symbol of sophisti-

cation and of the good life. The script of every film or stage play included offering cigarettes, lighting cigarettes, smoking and obviously enjoying them. Not only film stars but athletes and other public figures were seldom shown without a cigarette. One manufacturer advertised that his brand was the choice of two out of three doctors. Another made its fortune on the slogan, 'not a cough in a carload'. I understand that here in India your young people are being bombarded with this false claim of sophistication.

How different the situation in the USA is today! True, the tobacco industry still tries to identify smoking with the good life. One prominent campaign features the slogan 'Alive with pleasure' — a phrase which, as former Surgeon-General Koop recently told a Congressional committee, should be changed to 'Dying in agony'.

But the glamour has gone. Almost never today do we see a television or film star smoking. No self-respecting athlete would allow himself or herself to be publicly associated with tobacco products. Nonsmokers' rights have become a popular cause for politicians. The rapidly swelling tide of restrictions on smoking to which I have already referred is a direct consequence of this remarkable swing in society's perception of tobacco.

This swing of public opinion in less than a generation is especially remarkable when one considers that it has been accomplished with the expenditure of one public health dollar for every thousand tobacco industry advertising and promotion dollars. To turn one of the industry's favourite phrases back upon itself, 'We've come a long way!'

But please do not confuse this satisfaction with complacency. The tide may have turned, but the war is far from won. A year ago, on 11 January 1989, which was the 25th anniversary of the first Surgeon-General's Report, we issued a comprehensive summary entitled 'Reducing the Health Consequences of



Smoking: 25 Years of Progress'. The report contained five major conclusions. The first two stressed the progress that has been made. The last three emphasized the remaining challenges.

The first of these three areas of continuing concern is the target population groups. The conclusion states: "The prevalence of smoking remains higher among blacks, blue collared workers and less educated persons than in the overall population. The decline in smoking has been substantially slower among women than among men." Clearly, as we continue our educational efforts, we must give special attention to reaching these groups in our society. We need to do a better job of finding the media and framing the messages that reach them best. In this connection, I was pleased to learn that here in India your educational programme used a wide variety of media, ranging from films to folk-drama, to reach your diverse audiences.

The second of the remaining challenges is: "Smoking among high school seniors leveled off from 1980 through 1987 after previous years of decline." Here again, the moral is clear. If children are starting to use tobacco at younger and younger ages, then we must reach them with our message sooner. Antismoking curricula for elementary schools are available, well tested, and proven effective in preventing or deferring the initiation of smoking. But thus far, these curricula are not being systematically disseminated on a nationwide basis. Nor have we yet adequately explored the potential of mass media as a deterrent to smoking for young people.

The summary report's fifth conclusion states: "Smoking is responsible for more than one of every six deaths in the United States. Smoking remains the single most important preventable cause of deaths in our society." This we must never permit ourselves to forget. Even if tobacco usage were to cease on the stroke of midnight of the year 2000 — which it

surely will not — its residual effects would continue well into the 21st century. Continued tobacco use in the population will cause a great deal of human suffering for many decades.

You have been most patient during my recitation of the anti-smoking story in my own country. I have dwelt upon it at some length, in part because it is the story I know best and in part because I am proud of the progress we are attaining. But it is also my hope that those of you from India and other countries, and especially those from countries on the threshold of development, may learn something useful from our experience. As you increasingly confront the health problems of developed nations — especially those related to the environment and to health-related human behaviours — perhaps you can anticipate and avoid some of our mistakes. Perhaps you can set in motion at an earlier stage the kind of public policy which appears now, belatedly, to have turned the tide against tobacco usage in the USA.

The lesson we have learnt is that issues like the health consequences of tobacco cannot be solved by health and medicine alone: they are truly issues of public policy. Their resolution requires nothing less than Dr Nakajima's *grand alliance* of people, policy-makers and professionals.

I by no means intend to belittle the role of biomedical science. Knowledge based on solid research is the foundation of every beneficial public policy related to health. Research must continue. Its results must be proclaimed clearly, widely and repeatedly. Occasions must be sought or created to present relevant research findings both to a broad public audience and to specific target groups that are influential in policy formulation. Nor does it diminish the importance of the health care provider. His or her role is to provide credibility in matters related to health in daily personal contact with people's lives. His or hers is a triple responsibility — as practitioner, spokesperson



and role model. Policy-makers are more diffuse and harder to identify. Some are obvious — public figures who occupy key executive or legislative posts in government at various levels; others who may be equally influential in shaping public policies include corporate executives, communicators, educators, religious leaders and many more. But important as these policy-makers are, it is necessary to realize that many of them — especially those in the political arena — tend to be followers as well as leaders. This underscores the importance of the remaining partner in the *grand alliance* — the people themselves.

In relation to issues of smoking and health, we in the USA have witnessed an interesting phenomenon in the last few years — the spectacle of our so-called policy-makers running very hard to catch up with the will of the people. The proliferation of restrictions on smoking in public places and at work and the added excise taxes and other economic incentives to reduce tobacco usage have come as a result of a popular groundswell of opinion. Increasingly, with every passing year, smoking is becoming unacceptable as a social norm.

The changing policies reflect this attitudinal change in the society.

I am certainly not suggesting that our policies are without flaw. Clearly, for example, there is good reason for questioning a national policy that vigorously discourages tobacco usage by its citizens while encouraging tobacco production for export. But we have in fact come a long way in a short time, and I see every reason to believe that the trend will continue and that other countries can set in motion similar forces.

In conclusion, let me once again salute the Tata Institute of Fundamental Research for its pioneering work in the field of tobacco use and oral cancer and for its enduring leadership in research and the dissemination of research results. Let me salute also the scientific excellence represented here in this room and your individual and collective commitment to public health.

I believe that the bold goal of a smoke-free society is attainable in the not-too-distant future, and that its achievement will be the product of scientific excellence married to enlightened public policy.





# **TOBACCO PRODUCTION AND USE**





# Global aspects of tobacco use and its implications for oral health

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Tobacco originates from South America, where tobacco habits were practised long before Columbus discovered America. Since then, tobacco use in various forms has spread to all countries of the world. Tobacco is smoked in cigarettes, cigars, cheroots, *keeyos*, *kreteks* and water pipes; smokeless tobacco is used in various ways. Almost all forms of tobacco use lead to specific consequences for oral health.

## INTRODUCTION

The tobacco plant has existed for thousands of years in South America. When Columbus landed in the New World on 11 October 1492, he was offered golden tobacco leaves as a courtesy, but he threw them away. Some of his followers, it is said, picked up the leaves and brought them back to the Old World. Tobacco use spread with remarkable rapidity, and, in the course of time, different methods of using tobacco were developed. In this paper, we describe the methods of tobacco use practised in various countries.

## TOBACCO SMOKING

Tobacco smoking has been in vogue for hundreds of years, starting among the native populations of America. With the spread of tobacco to Europe and other parts of the world from the 16th century, tobacco smoking soon gained popularity.

**Cigarette:** Cigarette smoking is perhaps the most popular form of tobacco use in the western world, and it is spreading alarmingly fast to the Third World, even among children.

Cigarettes are made from fine-cut tobaccos which are wrapped in paper. Cigarette tobacco is a blend of different grades of flue-cured (Virginia), burley, Maryland and air-cured tobacco. Currently, a bewildering number of brands of cigarettes are commercially available throughout the world. The tar and the nicotine yields of cigarettes manufactured in different countries exhibit notable differences (1).

Cigarette smoking is injurious to health, including oral health: there is strong evidence linking smoking with oral cancer (1,2). The frequency, duration and mechanics of smoking play important roles in the pathogenesis of oral lesions. For instance, smoking cigarettes to a very small butt, which is common in China (Fig. 1A), produces leukoplakias in the labial mucosa (Fig. 1B). This lesion is similar to the leukoplakia associated with *hookli* (clay pipe) smoking in Bhavnagar district, Gujarat, India (3).

**Bidi:** Bidis are smoking sticks used extensively in the rural areas of several countries in South-East Asia, and especially in India. A detailed



description of this habit is given in the next paper (see Bhonsle *et al.*).



Fig. 1A. A Chinese smoking a cigarette to a small butt

Fig. 1B. Leukoplakia in the upper labial mucosa

**Cigar:** Although the prevalence of cigar smoking has decreased considerably over the last 15 years (1), it is still common in some countries. Smoking of large cigars is considered to be an American habit. Cigars consist of a filler, a binder and a wrapper, all of which are made from air-cured fermented tobacco. Cigars are factory made and vary in length and diameter. The pathogenesis of oral lesions associated with cigar smoking depends on the structure of the product.

**Cheroots** are small cigars made of heavy-bodied tobaccos, with both ends cut off. Cheroot smoking is popular in Denmark, especially among women (Fig. 2A). In that country, cheroot smoking is associated with leukoplakias (4) on the floor of the mouth (Fig. 2B). In a study of 368 leukoplakias in



Fig. 2A. A female cheroot smoker in Denmark

Fig. 2B. Leukoplakia in the floor of the mouth in a cheroot smoker

Denmark, 48 were situated in the floor of the mouth. Some 19% of leukoplakias among cheroot smokers were located in the floor of the mouth, as compared to only 10% among those



with other tobacco habits. The floor of the mouth is more vulnerable because of the extremely thin epithelium.

Cigar and cheroot smoking is also prevalent in other areas, with some regional variations. It is common in Burma (5), where even children indulge in this habit (Fig. 3A). In that region, cheroots (Fig. 3B) are made with very



Fig. 3A. A Burmese boy smoking a cheroot  
Fig. 3B. Different kinds of cheroots in Burma

coarsely cut tobacco. In a study of 6000 villagers, however, only one of the 101 leukoplakias was observed on the floor of the mouth.

A variant of the cheroot, known as *keeyo*, is also smoked in Burma (Fig. 4A) and neigh-

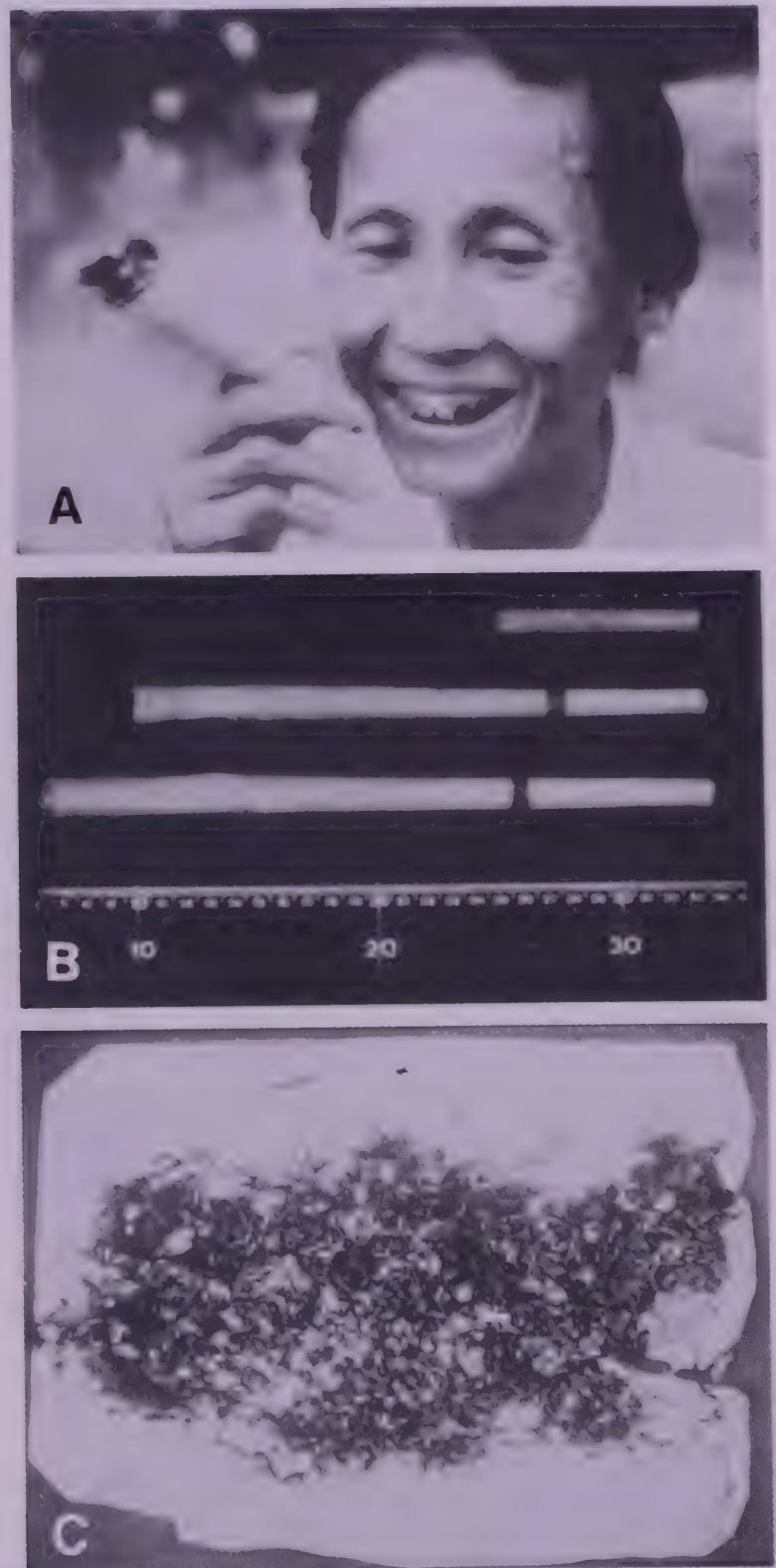


Fig. 4A. *Keeyo* smoker in Burma

Fig. 4B. *Keeyos* of different sizes

Fig. 4C. Contents of a *keeyo*: finely cut tobacco in a banana leaf

bouring Thailand. This cigar-like product, measuring up to 30 cm (Fig. 4B), is made by rolling a mixture of finely cut tobacco in the bark of the *keeyo* (*Streblus asper* L.) tree or in a



banana leaf (*Musa paradisiaca* L.) (Fig. 4C). The characteristic flavour of *keeyo* smoke is due to the outer covering. In a study of 1866 individuals in Thailand, 20% were *keeyo* smokers (6).

In the Chiang Mai area of northern Thailand, a cigar smoked mainly by women and measuring 8-10 cm is made by wrapping very finely cut tobacco in a corn leaf. In the study mentioned above (6), this form of smoking was practised by 4.5% of the 1866 individuals.

*Kreteks* (Fig. 4D) are indigenous cheroots containing tobacco, cloves and cocoa, which give the characteristic flavour and 'honey' taste to the smoke. *Kretek* smoking originated in Indonesia in 1824; the word *kretek* appears to have come from the sound and sparks produced when it is inhaled. This type of smoking is popular in rural areas; *kreteks* are cheap, can be bought singly, last for a long time and extinguish themselves automatically when they are put down. They are traditionally hand-made, but since the mid-1970s machine-made *kreteks* have been available commercially. The tar



Fig. 4D. *Kreteks* from Indonesia

and nicotine contents of *kreteks* are estimated to be two to five times higher than those in Australian cigarettes. *Kretek* smoking,

however, does not appear to be associated with oral lesions.

The habit of smoking cigars or cigarettes in reverse fashion, i.e., with the lighted end inside the mouth, is popular in several countries in South America, the Caribbean, Sardinia, the Dutch Antilles and some coastal areas of Andhra Pradesh and Goa in India. In many areas, reverse smoking is practised mainly by women (Fig. 5A); in Sardinia, however, it is popular among men (Fig. 5B). The origin of reverse smoking among men in this area dates back to mediaeval times when there

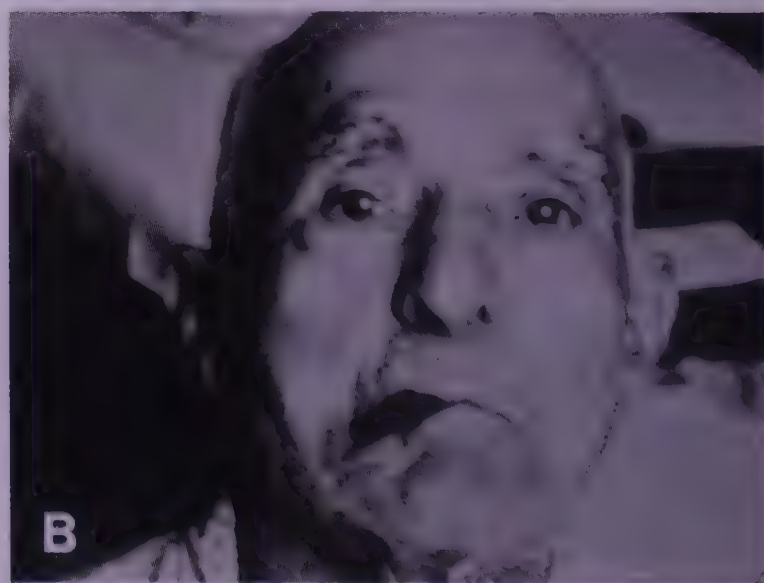


Fig. 5A. Reverse smoker in Colombia

Fig. 5B. Reverse smoker in Sardinia

were many civil wars in this region: when soldiers were on guard duty during the night they used this innovative method of smoking to avoid becoming victims of enemy snipers.



It is known that reverse smoking in the Indian state of Andhra Pradesh is responsible for palatal cancer and precancerous lesions (7-9) (see also paper by Daftary *et al.*, this volume).

**Pipe:** Tobacco is also smoked using various gadgets and types of tobacco. Pipe smoking is one such habit. It is one of the oldest, having been brought back to Europe by sailors from the Americas.

The different kinds of pipes used for smoking range from the European types, also used by tribal women in Chiang Mai (Fig. 6A), to the long-stemmed pipes used in China (Fig. 6B). Smoke drawn from a long-stemmed pipe is cooled because of the long distance it has travelled to reach the mouth. Perhaps for this reason, Chinese pipe smoking does not appear to produce precancerous oral lesions.

**Water-pipe:** Water-pipes include special receptacles through which the smoke has to



Fig. 6A. A Karen tribeswoman in Thailand smoking a European-style pipe

Fig. 6B. Smoking of long-stemmed Chinese pipe

Fig. 6C. A water-pipe made of bamboo, popularly used by the Karen tribesmen of Thailand

pass, ostensibly to reduce its harmful effects. A large variety of water-pipes are used in South-East Asia, in the Middle East and in Oceania (e.g., Papua New Guinea). They vary in size from the small ones used in Papua New Guinea to large, bulky water-pipes, as long as 100 cm, made of bamboo (Fig. 6C) and popularly used by the Karen tribesmen of Thailand. Smoking of water-pipes, especially the large ones, require great pulmonary effort. It does



not appear to produce precancerous oral lesions.

## SMOKELESS TOBACCO

The term 'smokeless tobacco' is used to describe tobacco that is consumed in unburnt form. Oral use of smokeless tobacco has existed for thousands of years in South America and has gained popularity in other areas as well. Smokeless tobacco is used in two ways: preparations are either placed in various parts of the mouth and sucked (dipping) or they are chewed. Smokeless tobacco products are made from dark or burley tobacco leaves, which are brown with golden highlights. These leaves are aged from one to three years to prepare chewing tobacco and for longer to produce snuff. It was estimated in 1984 that there were about 7-22 million smokeless tobacco users in the USA (10).

**Snuff dipping:** Snuff consists of finely cut or powdered, flavoured tobacco, prepared in three types: *dry snuff* is sold as a powder; *moist snuff* is made from uniformly cut, small particles of flavoured tobacco packed in moist form in flat containers; *fine-cut tobacco* is made from air- and fire-cured tobacco grown in the USA and is a coarser version of moist tobacco. Snuff is also marketed in sachets, which are popular among young adults in Scandinavia and the USA.

Snuff dipping consists of placing a pinch of snuff or a sachet in the gingivobuccal sulcus, with specific geographical variations. For instance, in Denmark, moist snuff is usually placed in the lower labial groove (Fig. 7A) for a varying length of time, which may be up to 10 h. Some people even sleep with snuff in their mouth. In contrast, in Sweden, where snuff dipping is much more widespread, the snuff is placed in the upper labial groove. The reason given for placing snuff in this location is to prevent its dilution by saliva and the consequent reduction of its effect. In the USA, snuff is used predominantly by women and is kept in the

mandibular groove. Snuff consumption is generally a male habit in Sweden and Denmark.

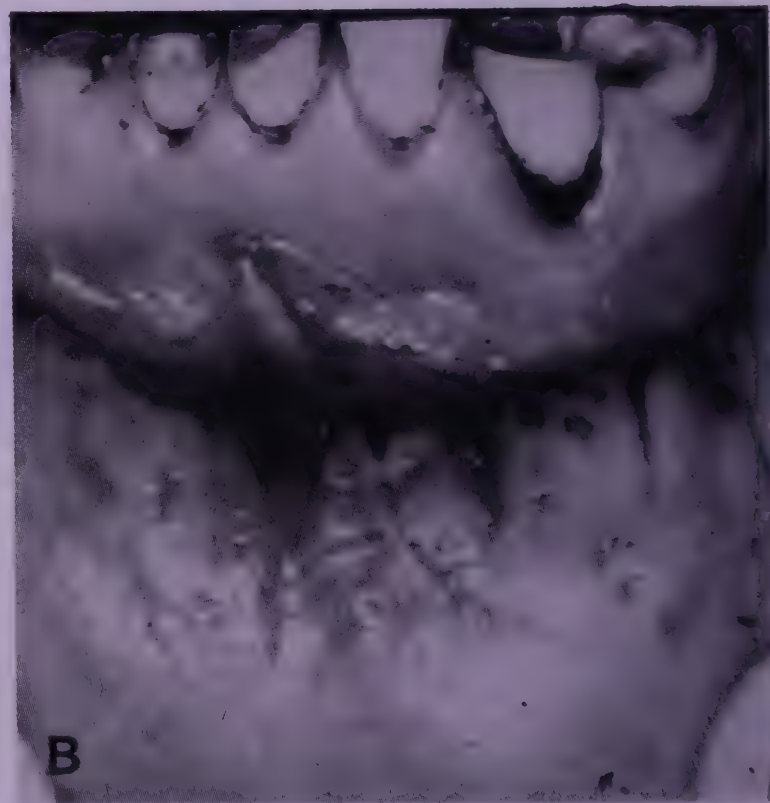
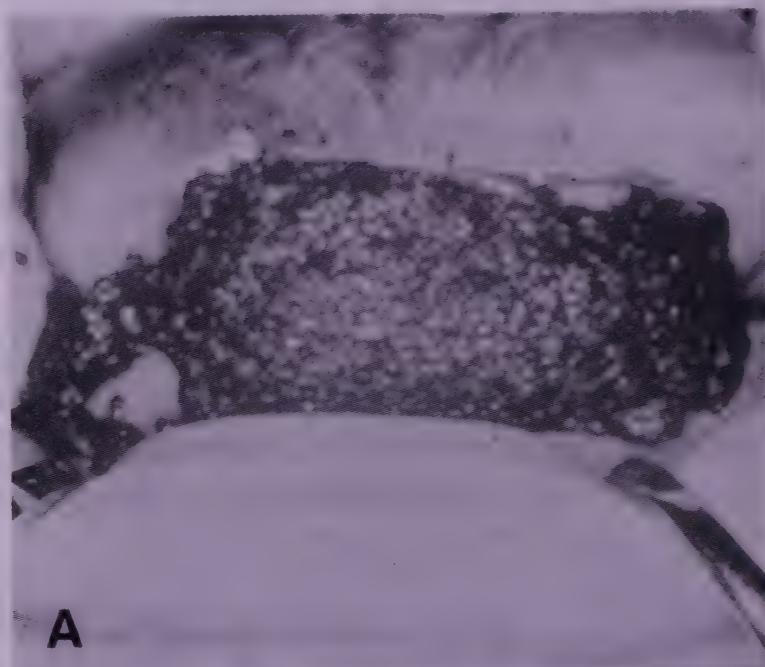


Fig. 7A. Snuff dipping in lower labial groove in Denmark

Fig. 7B. Snuff-induced leukoplakia: note the delicate striae

It was estimated in 1983 that there were 700 000-800 000 snuff users in Sweden (11). In Sweden and Denmark, the average snuff user is approximately 50 years old, uses snuff 10 h per day, has been using it for 22 years and consumes about 15 g per day (12-15).



Oral use of snuff produces leukoplakias (15) in the lower labial mucosa (Fig. 7B) in Denmark and in the upper labial mucosa in Sweden. Snuff-associated leukoplakias are homogeneous, with a wrinkled surface characterized by a very fine striated pattern; they are slightly elevated and diffusely demarcated from the surrounding normal mucosa. The striated appearance is due to the specific effects of snuff on the maturation of the epithelium, appearing histologically as focal areas of parakeratosis. These striae must be distinguished from the similar pattern seen in oral lichen planus. Because of this characteristic appearance, leukoplakias associated with snuff dipping are referred to as 'pumice stone type of leukoplakias'.

The type of snuff used seems to play an important role in producing different oral lesions. In Denmark, Gothenburg snuff, which is a mild snuff, is used and is generally associated with leukoplakias and very rarely with oral cancer. In contrast, in parts of the USA, Copenhagen snuff (Fig. 8) is used, which contains strong carcinogens (16).



Fig. 8. Copenhagen snuff

Snuff dipping or keeping finely cut tobacco with various ingredients in the mouth is prevalent in several parts of Africa, Asia and other regions. In South Africa, where snuff dipping is prevalent among Bantus, the product contains tobacco leaves and wet ash from

aloe plant leaves or from other species, with the occasional addition of oil, lemon juice and herbs. This preparation is somewhat alkaline (pH 8.2). Both men and women place this product in the lower labial groove. This snuff is mild compared to the Copenhagen snuff, and although the habit in South Africa is associated with a characteristic yellowish-white folded lesion at the site of placement of snuff, it does not seem to produce oral cancer. In Sudan, a strong, coarse preparation containing sun-dried, finely cut tobacco mixed with slaked lime is placed in the lower labial groove; this habit is associated with cancer of the lower labial mucosa.

*Naswar* use is prevalent in Afghanistan, Pakistan, Iran and a few Soviet Republics. Although there are some regional differences in the content of *naswar*, it is generally prepared from sun-dried, powdered tobacco, lime and indigo (Fig. 9A). It is made by pouring water into a cement-lined cavity to which lime is added, followed by air-cured, sun-dried, powdered tobacco. Indigo is added as a colouring material. The ingredients are then thoroughly pounded and mixed with a heavy wooden mallet.

In Afghanistan, *naswar* is taken in the palm of the hand and with a short, quick jerk on the lower lip, it is placed on the floor of the mouth (Fig. 9B). It is held in this position and sucked from time to time until it becomes bland.

The floor of the mouth is the most frequent location for oral cancer in Afghanistan. Similar observations have been made in Iran and the Soviet Republics where *naswar* is used.

**Tobacco chewing:** The habit of chewing tobacco alone is practised in the USA, Canada and Europe and in other countries. In the USA and Europe, three main types of chewing tobacco, firm plug/moist plug, loose-leaf (Fig. 10) and twist/roll, are used (17). *Plug* or *pressed-leaf tobacco* is made from enriched tobacco leaves or leaf fragments, wrapped in



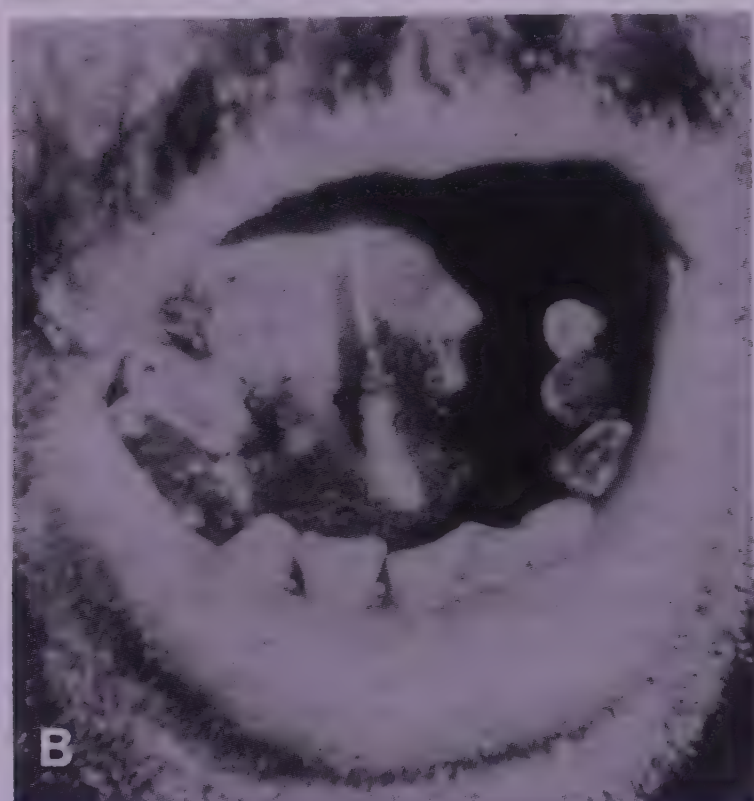


Fig. 9A. *Naswar* preparation in Afghanistan

Fig. 9B. *Naswar* placed in the floor of the mouth

fine tobacco and pressed into flat bars or rolls before being packed. Plug can be either firm or moist, depending on the moisture content. *Loose-leaf tobacco* is made of fermented cigar-leaf tobacco. Some brands are sweetened with various materials. The treated tobacco is packed as batches of loose pieces or cut strips. *Twist or roll tobacco* is made of cured leaf which has been treated with flavouring agents. The processed leaves are then twisted into strands and allowed to dry.

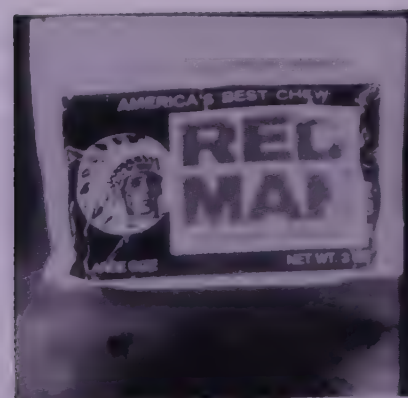


Fig. 10. Loose-leaf chewing tobacco in a foil pouch

The practice of chewing tobacco alone consists of placing a piece of tobacco in the mandibular groove and chewing it for a certain length of time. Terms such as 'chaw' and 'quid' are used to denote the size of the plug; a *chaw* is a wad of chewing tobacco the size of a golf ball, and a *quid* is usually a much smaller portion which is generally held in the mouth rather than chewed. A typical tobacco chewer in the USA is a male between the ages of 18 and 34 years, married, with high-school education or less (18). Chewing tobacco is preferred by many workers in heavy industries such as steel, coal and petroleum, where it is hazardous to smoke (17). Several studies have shown that tobacco chewing starts at an early age in the USA (see paper by Winn, this volume). Chewing of tobacco alone is known to be causally associated with oral cancer as well as with leukoplakia (19-21).

**Betel-quid chewing:** Betel-quid chewing is considered to be predominantly an Indian habit; it is also prevalent in several countries in Asia and in the Pacific region. An estimated 200 million people chew betel quid all over the world. The habit as practised in India is described in detail in the next paper in this volume; we limit our description to its practice in other areas.

As in India, the four basic constituents of the betel quids chewed elsewhere are betel leaves (*Piper betle*), areca nut (*Areca catechu*), slaked lime [ $\text{Ca}(\text{OH})_2$ ], and tobacco. In some areas, such as Papua New Guinea and the



South Pacific Islands, betel quid is chewed without the inclusion of tobacco.

In Indonesia, areca nut and betel leaves smeared with slaked lime are chewed first and then finely cut tobacco is added to the chew. While chewing the areca nut and betel leaves, the chewer cleans his or her teeth with the tobacco, and then places the saliva-soaked tobacco in the commissures of the mouth. This tobacco is generally re-used. Placement of a large amount of tobacco in this location may give a monstrous appearance (Fig. 11).



Fig. 11. Betel-quid chewer in Indonesia: note the monstrous appearance due to placement of tobacco in the commissures

The mechanics of betel-quid chewing in Papua New Guinea are also different. The nut from the fruit of the *Areca catechu* tree is separated and chewed; then slaked lime is taken from a beautifully decorated pumpkin calabash (Fig. 12A), with a spatula made of bone, and applied to the buccal mucosa (Fig. 12B). Many betel leaves are added to the quid, as is the stem of the *Piper betle*. Addition of the latter seem to give real enjoyment to the chewer.

The most serious outcome of chewing betel quid with tobacco is squamous-cell carcinoma. This habit also causes oral leukoplakia (9,22), which is precancerous (9,23).

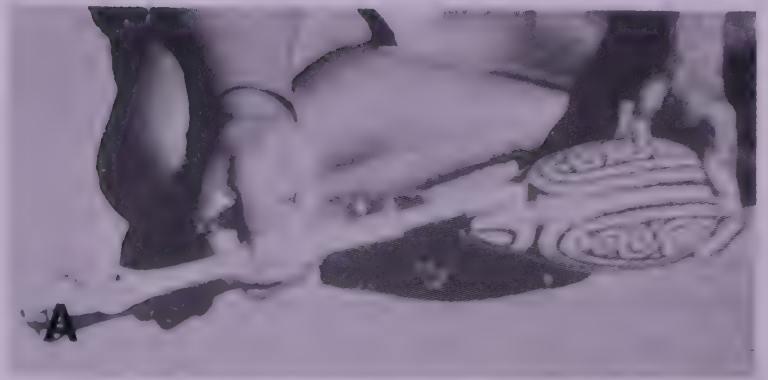


Fig. 12A. Betel-quid chewing in Papua New Guinea: taking slaked lime out of a calabash with a spatula

Fig. 12B. Application of lime to the buccal mucosa

As mentioned earlier, in Papua New Guinea betel quid is chewed without the inclusion of tobacco; however, oral cancer is also common in this region. This observation would indicate that chewing betel quid without tobacco is also carcinogenic; however, an epidemiological review of the carcinogenicity of betel-quid chewing with and without tobacco (24) pointed out that smoking of home-made cigarettes is also widespread in Papua New Guinea. Moreover, the excessive



use of slaked lime in this region causes a primitive burn on the oral mucosa, which might potentiate the action of smoking. The relative risks for oral cancer associated with chewing betel quid without tobacco are either insignificant or significantly lower than those associated with chewing betel quid with tobacco (24).

These findings do not, however, exonerate betel quid without tobacco: areca nut, one of the basic ingredients of betel quid, has been shown to be an etiological factor (25-27) for oral submucous fibrosis (see paper by Sinor *et al.*, this volume), which is a high-risk precancerous condition (23,28,29) (see also paper by Murti *et al.*, this volume).

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## Tobacco habits in India

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Following the introduction of tobacco into India by the Portuguese in about 1600, its use spread rapidly to all parts of the country, percolating into all sections of society. Tobacco is smoked, chewed, sucked or applied to teeth and gums in diverse ways. Many of these methods are specific to particular geographic regions. *Bidi* and cigarette smoking are practised widely in all regions. Other smoking habits include *chutta* and *dhumti*, which are also smoked in reverse (i.e., with the lighted end inside the mouth), *hookli* (clay pipe), *chilum* and *hookah*. Chewing tobacco in betel quid is the most popular form of smokeless tobacco use. Others comprise tobacco-lime mixture (*khaini*), tobacco-areca nut preparations like *mawa*, *mainpuri* tobacco and *pan masalas*. *Mishri*, *gudhaku* and creamy snuff are initially used as teeth cleaning material, but their use soon turns into addiction.

### INTRODUCTION

Tobacco was introduced into India by Portuguese traders in about 1600. It was thus first enjoyed in the capital city of Bijapur in the Adil Shahi Kingdom in South India along the trading route of the Portuguese. In 1604-05, Asad Beg, Ambassador of the Moghul Emperor Akbar, took a large quantity of tobacco from Bijapur to the Moghul Kingdom in the north and presented some to Akbar, along with a jewel-encrusted European-style pipe. He also gave tobacco and pipes to several nobles in the court. The tobacco was appreciated by everyone (see also under '*Hookah*' below), and its use spread swiftly to other sections of the society. It subsequently became an important item of trade. Although initially tobacco was only smoked, it was later chewed as well.

Various groups ascribed special virtues to tobacco, and within a short period it took deep roots in the socio-cultural milieu of the country. In the course of time, diverse methods of smoking and chewing tobacco were devised. This paper gives an overview on some of the

tobacco habits practised in India. Although each habit is described individually in this paper, they are practised in all possible combinations: one study of 10 000 individuals listed about 38 combinations of tobacco use prevalent in one region alone (1).

### PREVALENCE OF TOBACCO HABITS

No nation-wide survey has been made of the prevalence or types of tobacco habits practised in India. Considerable information is available, however, from large epidemiological studies, involving 158 000 villagers in seven areas of India (2-4), 35 000 dental out-patients in four urban centres (5-8) and other sources (9-11) (see paper by Luthra *et al.*, this volume).

The prevalence of tobacco habits shows considerable variation by area and gender (Table 1). The overall prevalence rates among men varied from 61% in Maharashtra to 86% in Andhra Pradesh; among women, it ranged from 15% in Bhavnagar to 67% in Andhra Pradesh. Men favoured both smoking and chewing, except in Pune, Goa, Uttar Pradesh

**Table 1**  
*Prevalence of tobacco habits (%) according to gender and area in India*

Area	Ref. no.	Men			Women		
		Smoking	Chewing	Total <sup>a</sup>	Smoking	Chewing	Total <sup>a</sup>
Bhavnagar (Gujarat)	2	62	15	71	<0.5	15	15
Ernakulam (Kerala)	2	67	36	81	2	39	40
Srikakulam (Andhra Pradesh)	2	77	11	81	64	3	67
Singhbhum (Bihar)	2	64	31	81	7	28	33
Darbhanga (Bihar)	2	50	54	78	45	11	52
Pune (Maharashtra)	3	8	55	61	<0.5	49	49
Goa	4	66	8	69	26	32	56
Mainpuri (Uttar Pradesh)	10	61	41	82	12	10	21
Maharashtra & Karnataka	9	46	49	84	—	—	—
Uttar Pradesh	9	26	68	82	—	—	—
Andhra Pradesh	9	23	70	86	—	—	—

<sup>a</sup>Those who smoked as well as chewed are included in both categories. *Mishri* and *gudhaku* are grouped under chewing.

—, data not available

and Andhra Pradesh, although there were some differences. In contrast, women preferred chewing except in Srikakulam and Darbhanga. Smoking was more prevalent among younger individuals and chewing among older age groups. The average age of male smokers in Ernakulam was 31.2 years and that of chewers, 52.1 years, while in Darbhanga it was 32.7 years for smokers and 41.1 years for chewers (2).

Studies of people in urban areas have been more selective, namely, of dental out-patients (5-8) and specific occupational groups, such as industrial workers (11). The prevalence rates are, however, comparable to those observed in rural areas. Although there are wide variations among regions, tobacco

smoking and chewing appear to be very common in urban areas as well.

## SMOKING

Inhaling and smoking of aromatic herbs for medicinal purposes was practised in India in as early as the 7th century, so that when tobacco was introduced as a smoking substance, it was naturally assigned medicinal qualities. By 1610, smoking had become extensive among both the nobility and commoners, even among women. In 1617, the Emperor Jahangir, the son of Akbar, decided that it produced adverse effects on the mental and physical health of his workers, and he promulgated draconian measures to stop it, such as ordering the lips of smokers to be slit (12). Despite this



royal antagonism, however, smoking continued to flourish.

Currently, smoking is practised in the form of cigarettes, *bidi*, *chutta*, *dhumti*, *hookli*, *chilum* and *hookah*. *Chuttas* and *dhumtis* are also smoked in reverse fashion, i.e., with the lighted end inside the mouth.

**Cigarette:** Cigarette smoking is primarily a western habit, and its introduction into India is due to western influence. The first Indian cigarette factory was established in 1906, and now a number of multinational and national companies manufacture about 100 brands of cigarettes (13), using about 30% of the tobacco produced in India (14). Cigarette consumption grew steadily until 1985, when it began to fall slightly, perhaps due to an increase in taxation

(see paper by Sanghvi, this volume). In terms of *per-caput* consumption, India ranks 102 among 110 countries surveyed (15).

There are several differences between Indian and foreign-made cigarettes. While in industrialized countries, emphasis is now on low-tar, low-nicotine, filter-tipped cigarettes, the tar and nicotine yields of Indian cigarettes are much higher (15). Unfortunately, there is no legal requirement for manufacturers in India to state the tar and nicotine yields of cigarettes. In India, only 15% of domestic cigarettes were filter-tipped in 1973, 29% in 1982 (15) and about 51% currently (see papers by Chari and Rao; Luthra *et al.*, this volume). In the USA, 85% of cigarettes were filter-tipped in 1973 and 93% in 1982 (15). The length of

**Table 2**

*Prevalence of various smoking habits among men in India<sup>a</sup>*

Habit	Prevalence of various smoking habits among											
	Gujarat		Kerala		Andhra Pradesh		Bihar				Goa	
							Singhbhum		Darbhanga			
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Bidi	2283	44	3046	62	662	12	2950	61	2043	42	1463	58
Cigarette	13	<0.5	286	6	132	2	23	<0.5	46	<0.5	137	5
Multiple habits	260	5	—	—	254	5	114	2	199	4	—	—
Hookli	569	11	—	—	—	—	—	—	—	—	—	—
Chilum	86	2	—	—	—	—	31	1	92	2	—	—
Hookah	21	<0.5	—	—	—	—	5	<0.5	87	2	—	—
Chutta	—	—	—	—	1030	19	—	—	—	—	—	—
Reverse chutta	—	—	—	—	2042	38	—	—	—	—	—	—
Pipe	—	—	—	—	—	—	—	—	—	—	64	3
Dhumti	—	—	—	—	—	—	—	—	—	—	4	<0.5
Others <sup>b</sup>	—	—	3	<0.5	—	—	6	<0.5	2	<0.5	—	—
No smoking	1995	38	1576	32	1229	23	1671	35	2390	49	847	34
Total	5227	—	4911	—	5349	—	4800	—	4859	—	2515	—

<sup>a</sup>Source: ref. (2,4)

<sup>b</sup>Others: Cigar, cheroot, etc.

filters on Indian cigarettes is only 12 mm compared to 20 mm in US cigarettes, and the amount of nicotine trapped in Indian filters is much lower (0.38-0.48 mg) than that in US brands (0.48-0.78 mg) (16). There is little difference in the nicotine yield of filter and non-filter cigarettes made in India (17).

Cigarette smoking is generally a male habit, and its prevalence in rural populations of India varies from 2-6% (Table 2). Cigarette

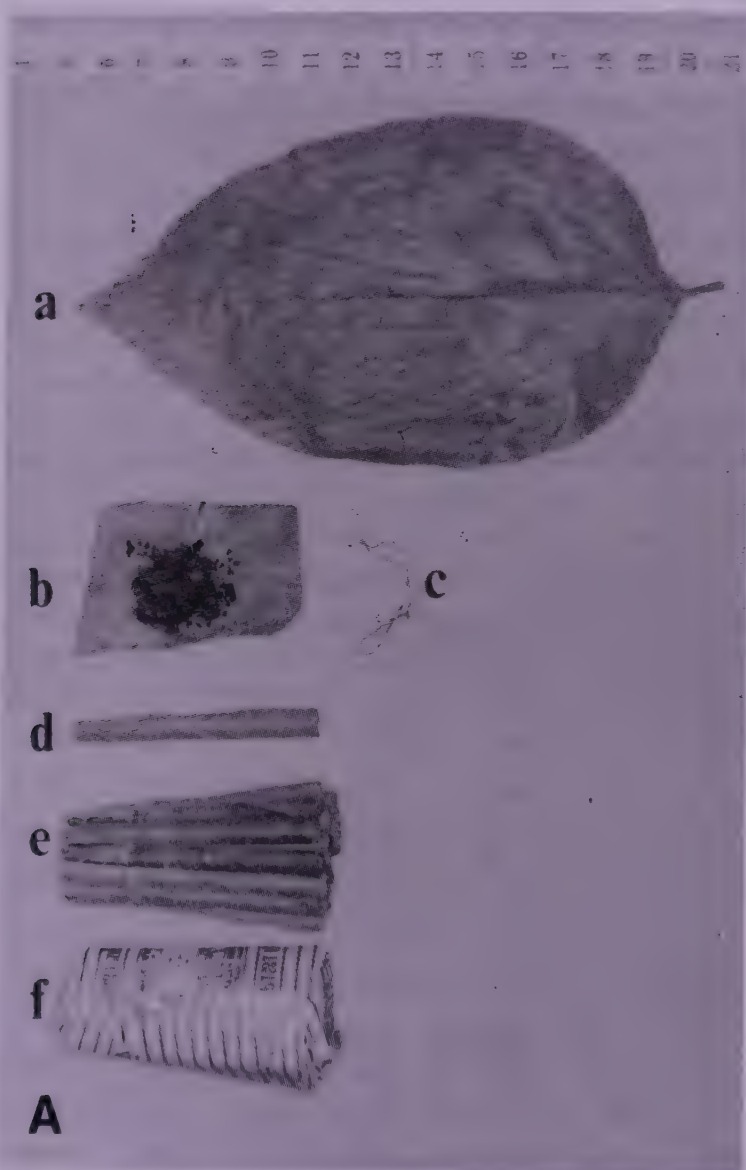


Fig. 1A. Preparation of *bidis*: (a) *temburni* leaf; (b) *bidi* tobacco on a cut *temburni* leaf; (c) thread to tie a *bidi*; (d) prepared *bidi*; (e and f) *bidi* bundles

smoking is far more popular in urban than rural areas and among the middle class.

**Bidi:** *Bidis* are the most popular form of tobacco use, consuming 34% of the tobacco

produced in India (14). They are made by rolling a dried, rectangular piece of *temburni* leaf (*Diospyros melanoxylon*) with 0.15-0.25 g of sun-dried, flaked tobacco into a conical shape and securing the roll with a thread (Fig. 1A). The length of a *bidi* varies from 4-7.5 cm; the diameter of the thicker end, which is the burning end, varies from 0.7-0.9 cm, and that of the flat end from 0.6-0.8 cm. *Bidis* are generally sold in bundles, each containing 8-24 *bidis*, but can also be purchased loose. On average, a *bidi* smoker smokes 8-15 *bidis* per day.

Some 60% of the weight of a *bidi* is made up of the *temburni* leaf wrapper. These leaves are used for rolling *bidis* because they are easy to work with when dried and are pliable and palatable when smoked; they resist early decay and are available in large quantities in forest tracts in some areas. The quality of these leaves depends on their texture and colour and the variation and thickness of the midrib and lateral veins. Fallen leaves are collected in summer, made into bundles of 50-80 leaves and dried further in sunlight for 3-6 days.

The flat end of the *bidi*, which contains hardly any tobacco, is kept in the mouth dur-



Fig. 1B. A *bidi* smoker



**Table 3**  
*Prevalence of various smoking habits among women in India<sup>a</sup>*

Habit	Gujarat		Kerala		Andhra Pradesh		Bihar				Goa	
							Singhbhum		Darbhanga			
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
<i>Bidi</i>	13	<0.5	43	<0.5	8	<0.5	222	4	714	13	351	12
Cigarette	—	—	—	—	—	—	—	—	—	—	3	<0.5
Multiple habits	3	<0.5	—	—	5	<0.5	24	<0.5	179	3	—	—
<i>Hookli</i>	2	<0.5	—	—	—	—	—	—	—	—	—	—
<i>Chilum</i>	1	<0.5	—	—	—	—	28	1	12	<0.5	—	—
<i>Hookah</i>	1	<0.5	—	—	—	—	24	<0.5	1536	28	—	—
<i>Chutta</i>	—	—	—	—	77	2	—	—	—	—	—	—
Reverse <i>chutta</i>	—	—	—	—	3002	62	—	—	—	—	—	—
<i>Dhumti</i>	—	—	—	—	—	—	—	—	—	—	187	6
Reverse <i>dhumti</i>	—	—	—	—	—	—	—	—	—	—	27	0.9
No smoking	4824	99	5333	99	1728	36	4950	94	3040	55	2366	81
Total	4844	—	5376	—	4820	—	5248	—	5481	—	2934	—

<sup>a</sup>Source: ref. (2,4)

ing smoking. Generally, people smoke by keeping the *bidi* (Fig. 1B) in one corner of their mouth or in the centre. *Bidis* are puffed more frequently than cigarettes, to prevent them from going out. Inhaling *bidi* smoke requires great pulmonary effort, perhaps due to its conical shape, small opening and poor combustibility due to the low porosity of the *temburni* leaf. *Bidis* produce a smaller volume of smoke than cigarettes (16,18), but, although they contain a small amount of tobacco (0.15-0.25 g compared to 1 g in a cigarette), they deliver as much as 45-50 mg of tar (19), as compared to 18-28 mg in an Indian cigarette (17). Furthermore, the mainstream smoke of a *bidi* contains much higher concentrations than that of US cigarettes of several toxic agents such as hydrogen cyanide (903 *vs* 445  $\mu$ g), carbon monoxide (7.7 *vs* 3.5 vol%), ammonia (284 *vs* 180  $\mu$ g), phenol (250 *vs* 150  $\mu$ g), other volatile

phenols (264 *vs* 173  $\mu$ g) and carcinogenic hydrocarbons like benz[*a*]anthracene (117 *vs* 81 ng) and benzo[*a*]pyrene (78 *vs* 47 ng) (19). *Bidis* also deliver more nicotine (1.74-2.05 mg) than Indian cigarettes (1.55-1.92) (17), probably because pure tobacco is used in *bidis*, while reconstituted tobacco sheets are used in cigarettes; the nicotine yields of these sheets are 1/6th to 1/10th of those of pure tobacco.

*Bidis* are smoked throughout India, especially in rural areas. Extensive house-to-house studies in such areas revealed that 12-62% of the men and 4-13% women practised this habit (Tables 2 and 3), although there appears to be a shift from *bidi* smoking to cigarette smoking.

**Cigar/cheroot/chutta:** These forms of tobacco are popular in certain regions of India (Fig. 2). Cheroots and *chuttas* are usually the



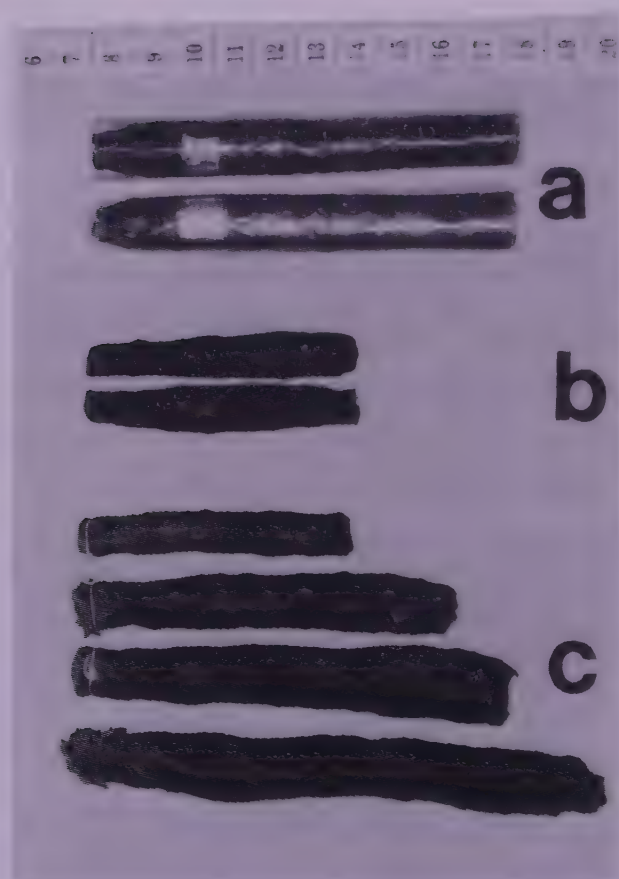


Fig. 2. (a) cigars; (b) cheroots; (c) *chuttas*

products of cottage and small-scale industry; *chuttas* may also be wrapped at home. Nearly 9% of the tobacco produced in India is used for making these products (14), and it is estimated that about 3000 million pieces of these products are made annually in this country (13).

*Cigars* are made of air-cured, fermented tobacco, usually in factories, and are more expensive than cheroots and *chuttas*. Cigar smoking is predominantly an urban habit.

*Cheroots* are small cigars made of heavy-bodied tobacco; they have no wrapper and contain a single binder. Cheroots were smoked by 2.7% of 10 000 villagers in a study in Ernakulam district, Kerala, conducted in 1967.

*Chuttas* are coarsely prepared cheroots. The name *chutta* in Telugu (spoken in Andhra Pradesh) may have come from the Tamil (spoken in Tamil Nadu) word *shruttu*, meaning 'to roll'. *Chuttas* are made by rolling a tobacco leaf into a cylindrical shape, one end of which is tied with a thread. The length of *chuttas* varies

from 5-12 cm. *Chutta* smoking is widespread in coastal areas of Andhra Pradesh, Tamil Nadu and Orissa. In one study among 5349 men and 4820 women in Andhra Pradesh, 19% and 2% practised this habit (Tables 2 and 3).

*Reverse chutta smoking*: The term 'reverse smoking' is used to describe the habit of keeping the lighted end inside the mouth (Fig. 3). This habit is practised extensively by women in rural areas of Visakhapatnam and Srikakulam districts of Andhra Pradesh. A typical smoker lights the *chutta* and draws a few puffs conventionally to ensure that it is properly lit. The lighted end is then placed in the mouth, leaving a small portion outside. Using negative pressure, the smoker draws frequently; if the *chutta* is going out, it is taken out and a few puffs are drawn conventionally. A person usually smokes one or two *chuttas* per day. Once lit, a *chutta* is smoked for a while, and allowed to go out for re-use.

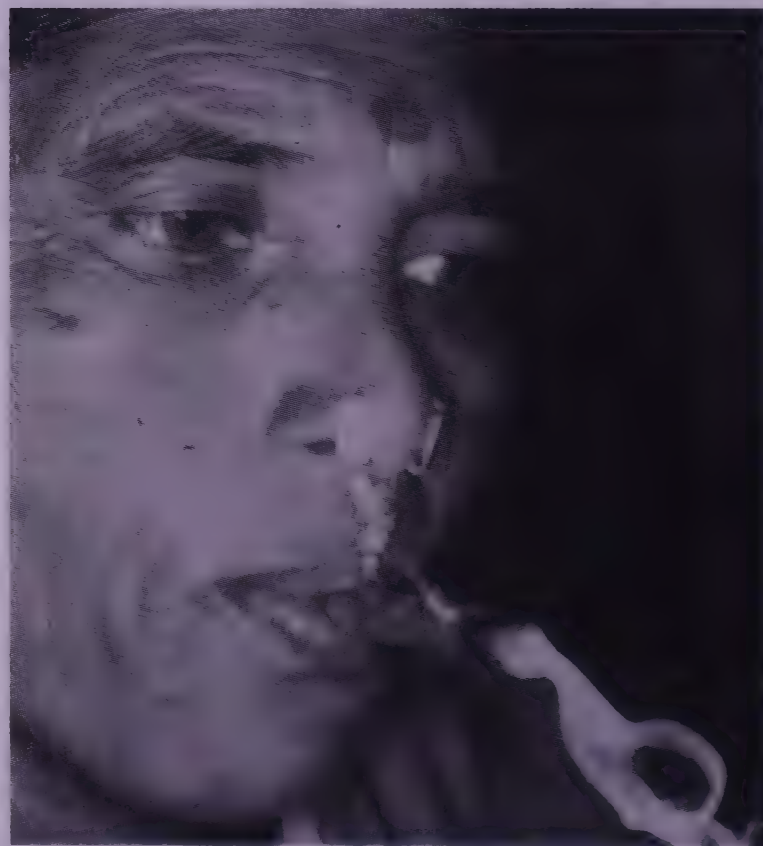


Fig. 3. A reverse *chutta* smoker

Several explanations have been advanced for reverse smoking: (i) Strong winds and splashing of water during household work



increase the chance that the *chutta* will be extinguished if smoked conventionally. This explanation might be valid since reverse smoking probably originated and is more common among fisherwomen. (ii) Women wanted to keep their smoking habit a secret from their husbands. This explanation can be given little importance, since smoking practices in a household cannot be kept a secret for long. It is nevertheless true that it is difficult to tell whether a reverse smoker is smoking or not if smoke is not blown out for some time, since only a very small portion of the *chutta* is visible. (iii) *Chuttas* are smoked in reverse to prevent the hot ashes from falling on children being nursed and on clothes. (iv) Reverse smoking relieves toothache and masks halitosis. The heat generated during such smoking may have a soothing effect. (v) Reverse smoking may have been perpetuated as a tradition. Children as young as 6-8 years may learn this habit when their mothers ask them to light *chuttas*, or mothers may actually coax their children to smoke in reverse as a remedy for various ailments.

In Srikakulam district, 46% of the 10 000 individuals surveyed smoked in reverse (2), and this habit was more common among women (62%) than men (38%) (Tables 2 and 3). Reverse smoking is more common in older than younger cohorts (2) and may be practised with other tobacco habits.

**Dhumti:** *Dhumtis* are a kind of a conical cigar made by rolling leaf tobacco in the leaf of a jack-fruit tree (*Artocarpus integrefolia* L.), occasionally in a dried leaf of a banana plant (*Musa paradisiaca* L.) or in the green leaf of a *hansali* plant (*Grewia microcos* L.) (Fig. 4A). The word *dhumti* might have originated from the Konkani (spoken primarily in Goa) word *dhumvore*, meaning smoke. Unlike *bidis* and *chuttas*, *dhumtis* are not available from vendors but are prepared by the smokers themselves.

In a random sample of about 5400 villagers in Goa, 4% were *dhumti* smokers (Tables 2

and 3). *Dhumtis* were smoked more often by Christians than people of other faiths, and 11% of Christian men and 19% of Christian

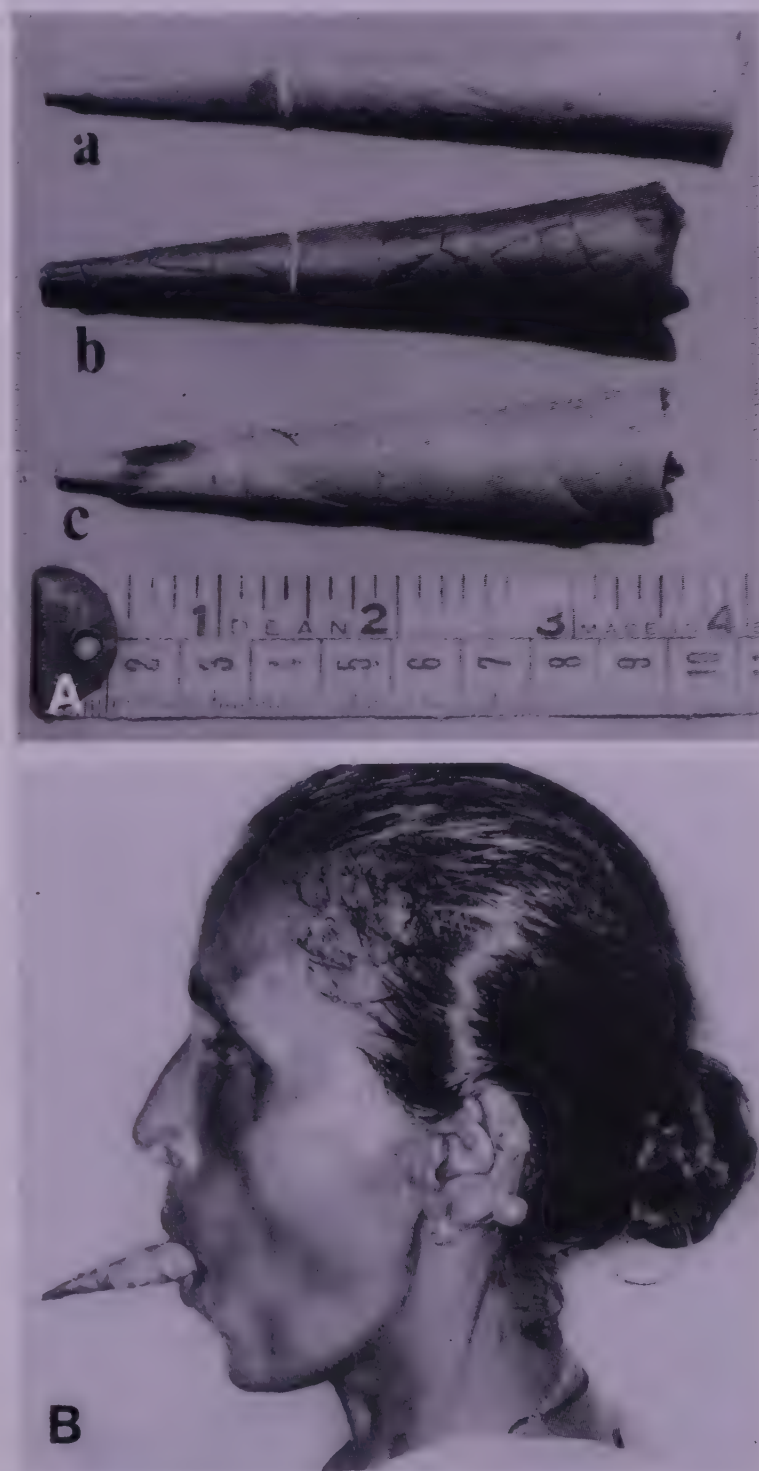
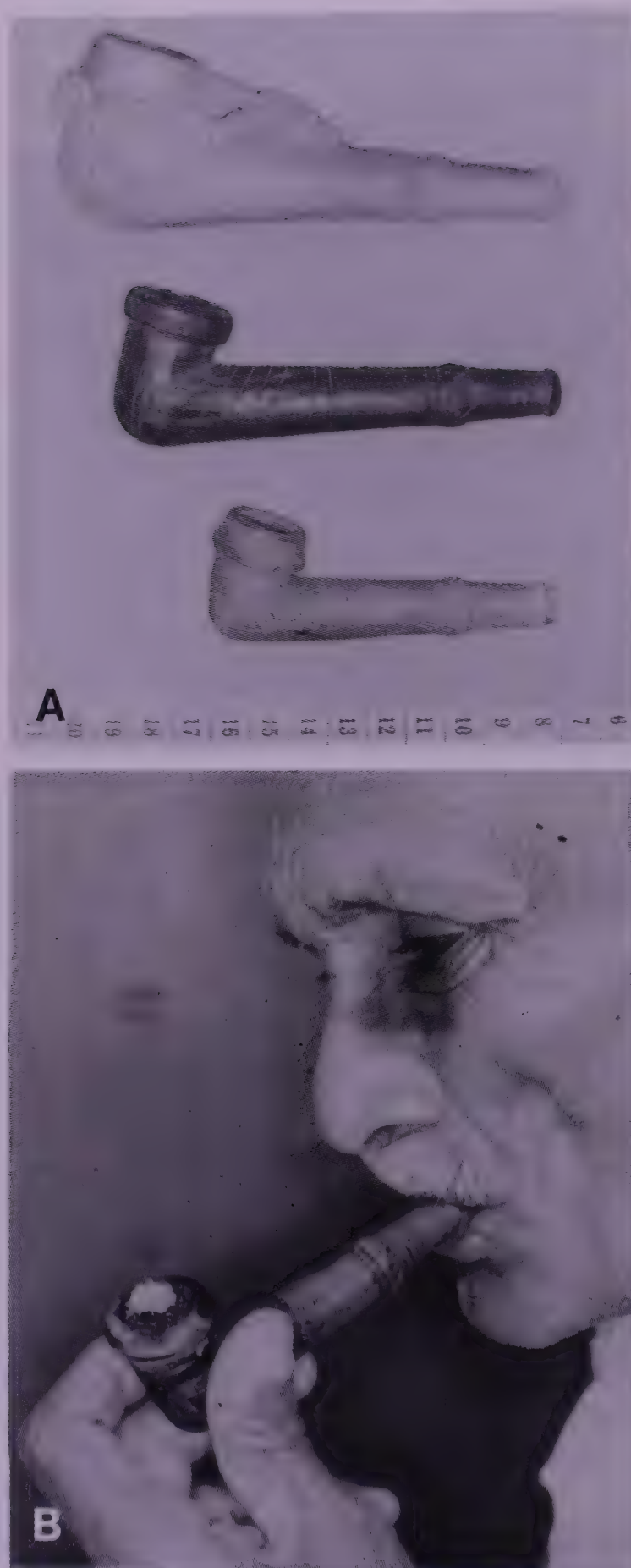


Fig. 4A. *Dhumti* preparations rolled in: (a) banana leaf; (b) *hansali* leaf; (c) jack fruit tree leaf

Fig. 4B. Reverse *dhumti* smoker

women (4) smoked one or two *dhumtis* per day. Once lit, a *dhumti* is puffed frequently; it may be allowed to go out for re-use, and is carried behind the ear by men and in the hair of women.



Fig. 5A. *Hooklis*Fig. 5B. *Hookli* smoker

*Reverse dhumti smoking:* *Dhumtis* are occasionally smoked with the lighted end inside the mouth (Fig. 4B). The overall prevalence of this

form of smoking is much lower (0.5%) (4) than that of reverse *chutta* smoking (46%) (2).

***Hookli:*** *Hooklis* are clay pipes commonly used in the Bhavnagar district of Gujarat (Fig. 5A). The stem is 7-10 cm long, with a mouthpiece; sometimes, a wooden stem is used, with a detachable clay bowl, presumably to reduce the heat. Interestingly, American Indians and the Englishmen of the Elizabethan era used clay pipes.

Prior to filling the *hookli* with tobacco, the smokers put a pebble or a stopper into the bowl to prevent tobacco from entering the stem during smoking. Usually, approximately 1.5 g of sun-dried tobacco in flake or powdered form moistened with molasses is taken in the palm and stuffed firmly into the bowl. Once the pipe is lit, it is smoked intermittently; on average, 15 g of tobacco are smoked daily. During smoking, the pipe stem is held in the centre or on either side of the mouth (Fig. 5B). *Hookli* smoking generates heat that can be felt at the stem. This habit was practised by 11% of the 5227 men in Bhavnagar district of Gujarat (Table 2).

Fig. 6A. *Chilums*

***Chilum:*** The *chilum* is a straight, conical pipe made of clay, 10-14 cm long (Fig. 6A). It is held vertically and, to prevent the tobacco from entering the mouth, a pebble or stopper is inserted into the top of the *chilum*. The entire



pipe is usually filled with tobacco similar to that used in *hooklis*. The narrower end, which serves as a mouth-piece, is wrapped with a wet



Fig. 6B. *Chilum* smoker

piece of cloth to protect the mouth from the heat and to serve as a filter.

*Chilum* smoking is an exclusively male habit (Fig. 6B), limited to the northern states of India, predominantly in rural areas. In one study among 5227 and 4859 men in Bhavnagar and Darbhanga districts, 2% in each area smoked a *chilum* (Table 2). In a survey based on 35 000 individuals in Mainpuri district, Uttar Pradesh, 28% of the villagers were estimated to be *chilum* smokers (10). In urban Lucknow, Uttar Pradesh, only 0.6% of the 10 000 dental out-patients smoked *chilum* (1). *Chilum* smoking requires a deep pulmonary effort. Often, one *chilum* is shared by a group. They are made locally, are inexpensive and easily available; they are also used for smoking opium and other narcotics.

**Hookah:** The *hookah* is an Indian water pipe, the origin of which corresponds to the introduction of tobacco in India (12). When Emperor Akbar received the gift of tobacco and a pipe, he took a few puffs out of curiosity and courtesy, but his physician forbade him to inhale the smoke from tobacco, which was an unknown substance. He suggested that if the smoke were passed through water, it might become safer. The result was the creation of the *hookah*. Perhaps because of its origin and its patronage by Moghul rulers, this form of smoking became popular in parts of India where a strong Moghul influence prevailed; it was especially favoured among men and women of the aristocratic and elite classes both in the areas of Moghul influence and in North India. *Hookah* smoking thus became a part of the culture, and sharing of a *hookah* became associated with social acceptance, brotherhood and equality. To this day, the expression for social boycott in North India is to stop sharing the *hookah* and water from the village well.

The *hookah* (Fig. 7A and B) consists of a receptacle for water which has an opening on the top to which a long wooden stem is fixed; at the top of this stem, a small bowl is attached for tobacco. A long flexible tube is fixed to an outlet on the side of the receptacle, through which the tobacco is smoked. Cut, shredded tobacco moistened with molasses is kept in the bowl and burned with charcoal. The smoke is drawn through the water, which cools and filters it (Fig. 7C). *Hookah* smoking also requires deep inspiration.

A wide variety of *hookahs* is available. The expensive varieties, used by affluent people in rural areas of northern and eastern India, consist of ornate brass receptacles and bowls, with embroidered smoking tubes. Commoners use inexpensive types in which the water receptacle is made of a coconut shell and the tobacco bowl of clay. Sometimes, the flexible tube is replaced by a wooden tube, or the tobacco is smoked directly from the outlet.

Water is reported to be a relatively effective filter, which reduces the tar content of the

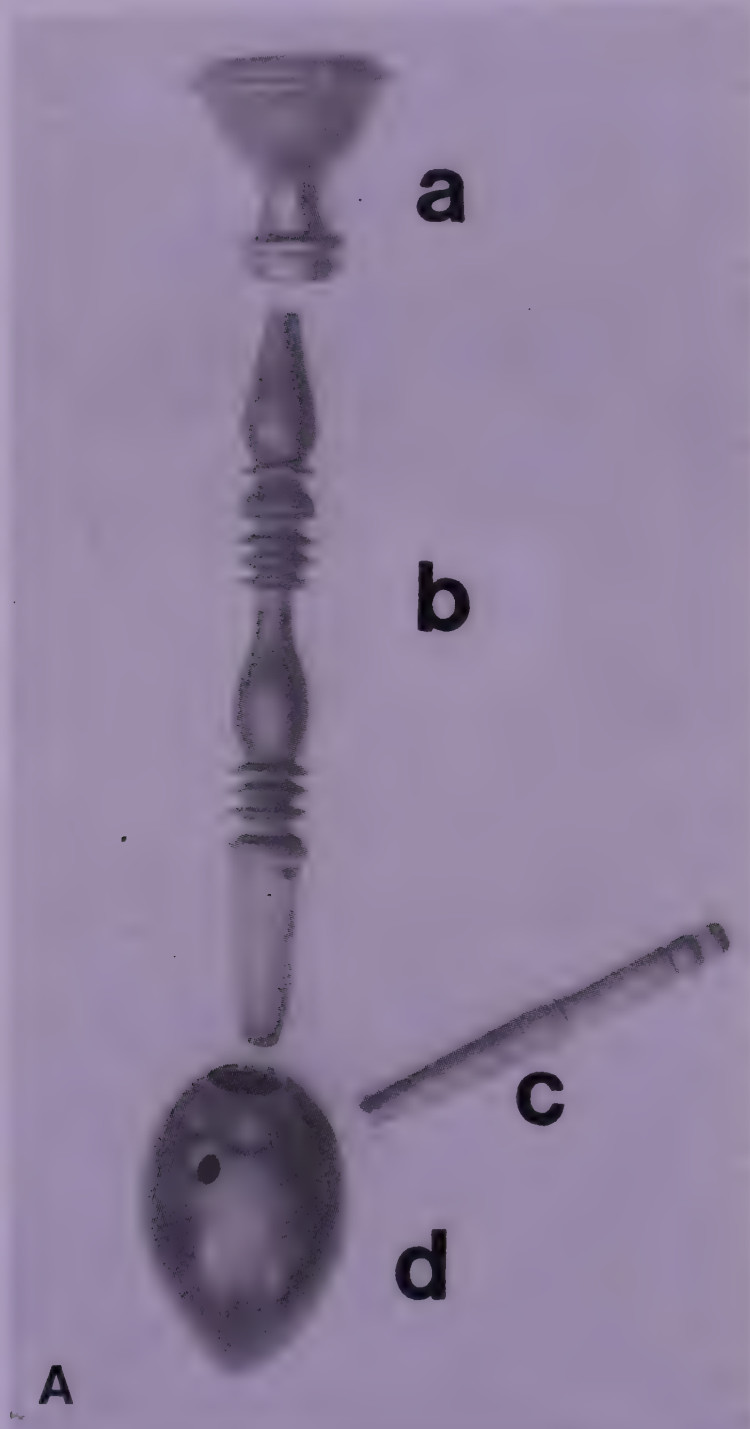


Fig. 7A. A hookah: (a) clay bowl to hold tobacco; (b) wooden stem; (c) wooden smoking tube; (d) coconut-shell water receptacle

smoke and chemical analysis of *hookah* smoke places it on a par with smoke from the mildest cigarette; the levels of carbon monoxide and other non-water-soluble toxicants are not reduced. The *hookah* is also an efficient mode of spreading tuberculosis (20).

In Lucknow, Uttar Pradesh, 3.8% of the 10 000 dental out-patients were *hookah* smokers

in combination with other tobacco habits (1). In a study of 622 individuals in rural Bihar near Patna, 18% smoked the *hookah*, and 95% of these were women (21). In Mainpuri district, Uttar Pradesh, 7% of the estimated 300 000 villagers were *hookah* smokers (10). In a random sample of 4859 men and 5481 women in Darbhanga district, Bihar, 2% and 28% smoked the *hookah* (Tables 2 and 3). The reason given for this female predominance is that it is inconvenient for men to carry a *hookah*, whereas women remain at home most of the time. Judging from the fall in the consumption of *hookah* tobacco (see paper by



Fig. 7B. Assembled *hookah*



Sanghvi, this volume), *hookah* smoking appears to be on the decline in India.



Fig. 7C. Hookah smoker, note the long smoking tube

### SMOKELESS TOBACCO USE

Oral use of smokeless tobacco is widely prevalent in India; the different forms include chewing, sucking and applying tobacco preparations to the teeth and gums. Smokeless tobacco products are often made at home but can also be purchased. Recently, a variety of smokeless tobacco products has become available in plastic and aluminium foil packets and in tins. About 19% of the tobacco produced in India is used to make smokeless tobacco products (14). Tobacco used for these purposes is prepared by harvesting the tobacco leaves when they turn yellow and brownish spots start appearing, leaving the leaves in the field for uniform drying, tying them into bundles moistened with water or molasses and storing them for fermentation for a couple of weeks. The bundles are then separated and dried again, and the leaves are cut into various sizes. Smokeless tobacco contains several carcinogenic products (see paper by Hoffman *et al.*, on smokeless tobacco, this volume).

**Pan (betel quid) with tobacco:** *Pan* chewing, commonly known as betel-quid chewing, is often erroneously referred to as 'betel-nut chewing'. This habit is of great antiquity, and literary sources indicate that it has existed in India for over 2000 years. Historical evidence from stone inscriptions exists from the year 473 AD. Some scholars believe that *pan* chewing was introduced into India from the South Sea Islands, Java and Sumatra, through maritime trading contacts. In Hindu (the predominant religion in India) culture, *pan* chewing is described as one of the eight *bhogas* (enjoyments) of life. Chewing of *pan* results in the formation of bright-red juice which colours the mouth; this was considered to be cosmetic, especially for women. In an excellent historical, religious and cultural perspective of *pan* chewing, Gode (22) mentioned that in the Hindu *Dharma Sastra* (code of behaviour), the areca nut pleases the *God Brahma* (the creator), the betel leaves pay homage to *Vishnu* (the protector), and slaked lime bows to *Siva* (the destroyer). Ancient scriptures stipulate the number of betel leaves with which a *pan* must be made for specific individuals or use. Interestingly, the scriptures forbid the use of *pan* by people who adopt a religious mode of life or observe vows, by widows, by menstruating women and by students.

*Pan* chewing was adopted by invading kings and settlers in India. It was also a part of the Moghul culture: several Moghul rulers were great connoisseurs of *pan* and employed specialists skilled in preparing *pans* to suit all occasions. Thus, the social acceptance and importance of *pan* did not decrease even during the Muslim era.

*Pan* consists of four main ingredients — betel leaf (*Piper betle*), areca nut (*Areca catechu*), slaked lime [ $\text{Ca}(\text{OH})_2$ ] and catechu (*Acacia catechu*). Condiments and sweetening agents may be added. Some time after its introduction, tobacco became an important constituent of *pan*, and currently most habitual *pan* chewers include tobacco (Fig. 8A and B). In

**Table 4**  
*Prevalence of different forms of smokeless tobacco use among men in India<sup>a</sup>*

Habit	Gujarat		Kerala		Andhra Pradesh		Bihar				Goa	
							Singhbhum		Darbhanga			
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Pan with tobacco	101	2	1640	33	245	4	84	2	301	6	144	6
Pan without tobacco	242	5	15	<0.5	134	3	—		—		48	2
Tobacco with lime	300	6	—		2	<0.5	1308	27	2149	44	—	
Tobacco alone	30	<0.5	104	2	484	9	9	<0.5	6	<0.5	12	<0.5
Bajjar	52	1	—		—		—		—		—	
Gudhaku	—		—		—		54	1	—		—	
Multiple habits	7	<0.5	—		3	<0.5	35	<0.5	24	<0.5	—	
Areca nut	68	1	—		—		3	<0.5	184	4	—	
No chewing habit	4427	85	3152	64	4481	84	3307	69	2192	45	2311	92
Total	5227		4911		5349		4800		4856		2515	

<sup>a</sup>Source: ref. (2,4)

**Table 5**  
*Prevalence of different forms of smokeless tobacco use among women in India<sup>a</sup>*

Habit	Gujarat		Kerala		Andhra Pradesh		Bihar				Goa	
							Singhbhum		Darbhanga			
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Pan with tobacco	1	<0.5	1881	35	135	3	71	1	96	2	780	27
Pan without tobacco	6	<0.5	41	<0.5	25	<0.5	—		—		131	4
Tobacco with lime	5	<0.5	3	<0.5	—		512	10	371	7	—	
Tobacco alone	5	<0.5	118	2	116	2	7	<0.5	—		18	1
Bajjar	666	14	—		—		—		—		—	
Gudhaku	—		—		—		833	16	—		—	
Multiple habits	—		—		2	<0.5	23	<0.5	—		—	
Areca nut	12	<0.5	2	<0.5	—		1	<0.5	68	1	—	
No chewing habit	4149	86	3331	62	4542	94	3801	72	4946	90	2005	68
Total	4844		5376		4820		5248		5481		2934	

<sup>a</sup>Source: ref. (2,4)





Fig. 8A. A betel-quid preparation

six areas in India, encompassing 56 000 villagers, *pan* was chewed more often with tobacco (Tables 4 and 5). *Pan* chewing induces euphoria, increases salivation, and is said to possess anti-helminthic properties.

*Betel leaves* are an indispensable part of *pan*. They are cultivated under hot and humid conditions in almost all states of India, except the dry north-west. The betel vine is a creeper, and it is often grown next to areca-nut trees, which provide support, or on wooden scaffoldings. A crop lasts for 3-12 years, and each vine is picked three to five times each year. The picked leaves are cleaned, counted and sorted into batches depending on the size, colour, texture, maturity and position on the betel vine. Different types of leaves are known by different names in various areas. Betel leaves are also bleached, to improve their quality and taste, by leaving tender leaves in a warm, ventilated place without direct sunlight.

Betel leaves contain volatile oils, such as eugenol and terpenes, nitrate and small quantities of sugar, starch, tannin and several other substances.

*Areca nut* is obtained from the fruit of the *Areca catechu* tree. The outer pericarp of the ripe fruit, which is orange-yellow, is removed to separate the nut, which is used fresh in Kerala,

Karnataka, West Bengal and Assam, and after sun-drying, curing or baking elsewhere in India. Curing consists of boiling the sliced kernel with a little extract from the previous year's curing; this results in a uniform colour, softens the nut and reduces the tannin content. About 75% of the marketed produce is consumed after processing. Areca nuts are graded depending upon the processing method, and are known by various names. Processing also results in variations in the relative proportions of the constituents of areca nuts.

The two important constituents of areca nut are tannins (11-26%) and alkaloids (0.15-0.67%). Arecoline is the principal alkaloid (0.5-0.7%); fats, carbohydrates and various other substances are also present. Areca-nut alkaloids can give rise to carcinogenic nitrosamines in the presence of salivary nitrites (23).

Areca nuts are cultivated on about 184 500 ha in India, with a production of 191 400 tonnes of nuts. More than 400 000 people depend on areca nut-related activities (24).

*Slaked lime*: Lime ( $\text{CaO}$ ) is either prepared from sea shells or quarried from limestone ( $\text{CaCO}_3$ ). *Shell lime* is made from the calcareous or silicious covering of marine invertebrates harvested along the coast of India. The shells are roasted on a fire, and water is sprinkled to powder them; more water is added to make slaked lime paste. *Stone lime* is quarried in central India. The pH of the two types of lime is the same. Lime is manufactured in small-scale industries. Commercially available brands may be coloured and flavoured.

*Catechu* is the residue of a hot-water extraction of the heart-wood of the *Acacia catechu* or *A. suma* tree. After cooling, catechin crystallizes out, leaving the more soluble catechu tannic acid solution. The main constituents of catechu are tannins (25-35%) and polyphenols (23).



*Tobacco* is the most important ingredient of *pan* for regular users. Various tobacco preparations are used:

In Kerala, raw tobacco is included in *pan*. It is marketed in bundles containing several strands, each about 115 cm long and 5 cm thick. A regular user consumes one 15-cm piece of the strand per day.

In the Kannada language (spoken in Karnataka), *kaddipudi* means 'powdered sticks'. This is the cheapest form of tobacco, made by crushing the stalks and petioles of the tobacco plant into a fine powder. It is used either as the powder or in a processed form, as bricks and blocks made with *jaggery* (sugar molasses) and water.

*Hogesoppu* is a leaf tobacco used frequently by women in Karnataka, either by itself or with *pan*.

*Gundi* is a mixture of cured tobacco, coriander seeds and other spices. Each constituent is fried separately, powdered coarsely and mixed and the product is scented with a resinous oil. *Gundi* is known as *kadapan* in Orissa and Bengal; it is also used in Gujarat.

*Zarda*, *pattiwala* tobacco and *kiwam* are popular tobacco preparations, especially in northern India.

*Zarda* is prepared by cutting tobacco leaves into small pieces and boiling them in water with slaked lime and spices until the water evaporates. It is then dried, and colouring and flavouring agents are added. *Zarda* may be chewed by itself, with areca nut or in betel quid. It is available in small packets or tins.

*Pattiwala* is a sun-dried, flaked tobacco which may be used with or without lime.

*Kiwam* is a thick tobacco paste; it is also available as granules or pellets. To prepare *kiwam*, the midribs and veins of tobacco leaves are removed, and the remaining matter is boiled in water. Powdered spices (saffron,

cardamom, aniseed and musk) are added, and the mixture is stirred and allowed to macerate until it becomes a paste, from which granules and pellets are made.

*Preparation of pan (betel quid)*: *Pan* can be purchased in a prepared form from innumerable vendors and kiosks. Depending on the size of the leaf and regional preferences, whole, partial or multiple betel leaves are smeared with lime and catechu. A few pieces of areca-nut preparation (see below) and the preferred tobacco are added. According to personal choice, cardamom, clove, camphor, other condiments, herbal medicines, gold dust and even aphrodisiacs may be added. The preparation is then folded into various ornate shapes and given to the customer.

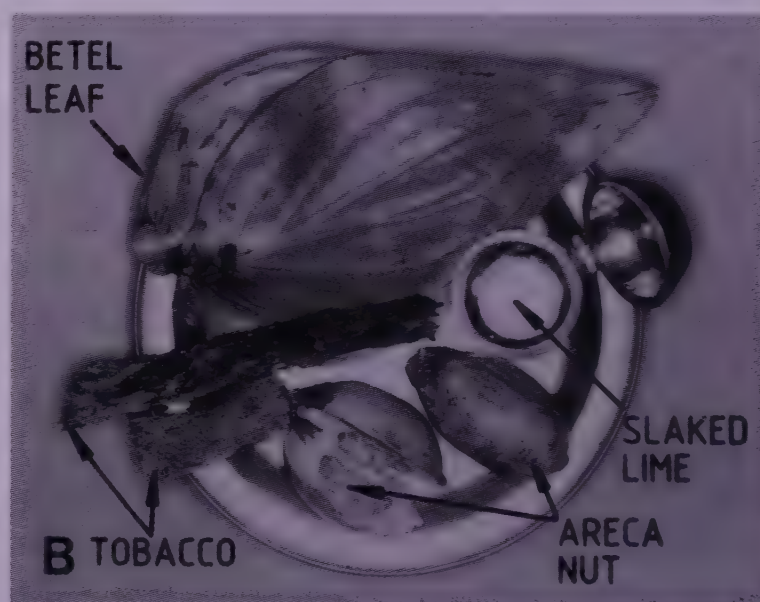


Fig. 8B. Constituents of *pan* in Kerala

A regular user requires a steady supply of *pan*. Affluent people in urban areas buy prepared *pans* from kiosks and carry them in a container. Most other people buy the main ingredients of their choice in retail shops and make *pan* themselves as needed. In rural areas, the ingredients are carried in a cellophane wrapper and prepare *pan* as and when required.

Regional differences in the choice of material and the way in which *pan* is chewed abound. For example, in Kerala, raw areca



nut, tobacco and shell lime are preferred (Fig. 8B). Typical users smear one or two betel leaves with shell lime and place them in their mouths. While chewing, a few pieces of raw areca nut are cut and added to the 'chew'. About 5 g of tobacco from a strip are then snapped off by hand or cut with a knife and added to the bolus in the mouth. Thus, in contrast to *pan* prepared by vendors, the ingredients are placed individually in the mouth and chewed. The bolus is kept in the mandibular groove. On average, a person may chew five to ten times a day.

*Pan* chewing produces excess saliva which, if the *pan* does not contain tobacco, is generally swallowed. When *pan* is chewed with tobacco, saliva is spat out from time to time. The bright red colour produced during the chewing of *pan* is due to the formation of *o*-quinone from water-soluble polyphenols, notably leucocynidins, at the alkaline pH of 8-9 via secondary reactions (24).

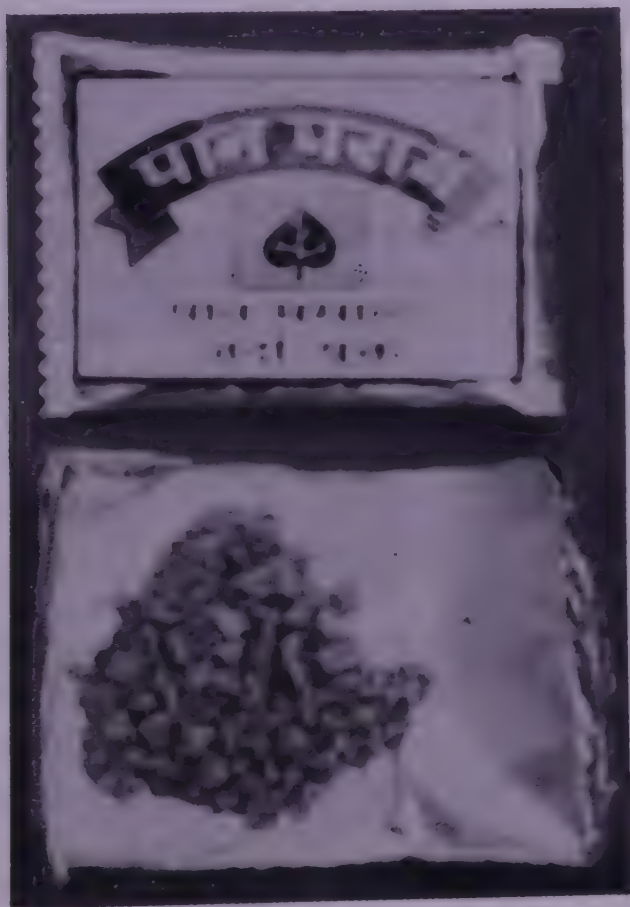


Fig. 9. *Pan masala* with tobacco in a foil pack

***Pan masala:*** *Pan masala* is a commercial preparation containing areca nut, slaked lime,

catechu and condiments, with or without powdered tobacco (Fig. 9). This preparation has been marketed since 1975, and recently there has been an advertising blitzkrieg on the television and in the press. Although advertising of tobacco products on radio and television is banned, there is no restriction on the advertisement of *pan masala* without tobacco; however, the brand names of *pan masala* with and without tobacco are identical. Aggressive advertising, targeted at the middle class and youth, is believed to have enhanced the sales of this product.

*Pan masala* contains many of the ingredients of *pan*, but it is not perishable. It comes in attractive foil packets (sachets) and tins, which can be stored and carried conveniently. Carrying a *pan masala* tin has even become a status symbol, and offering *pan masala* is accepted as implying hospitality and equality.

*Pan masala* is very popular in urban areas and is fast becoming popular in rural areas. Although the actual prevalence of this habit is not known, its popularity can be gauged by production figures: according to an estimate in a leading business magazine in 1990 (25), the Indian market for *pan masala* is worth Rs. 2000 million (US\$ 116 million), and in North India alone there are 150 *pan masala* plants. *Pan masala* is also marketed in about ten countries in Europe, in the Middle East, in the USA, in Japan, in Australia and in South-East Asia. One leading Indian firm, with a 60% market share, exported Rs. 500 million (US\$ 29 million) worth of *pan masala* to these areas in 1989-90.

The introduction of 4-g aluminium foil sachets (Rs. 1.50 or US\$ 0.05) seems to have boosted sales tremendously. One leading brand registered a 40-fold increase in sales within one year following the introduction of such sachets. Currently, 500-600 million sachets of one popular brand are sold annually.



**Tobacco, areca nut and slaked lime preparations:** Combinations of tobacco, areca nut and slaked lime are chewed in several regions in North India, where they are known by different names.

**Mainpuri tobacco:** In the Mainpuri district of Uttar Pradesh and in nearby areas, this preparation is very popular. It contains mainly tobacco, with slaked lime, finely cut areca nut, camphor and cloves (Fig. 10). In a study of 35 000 individuals in the Mainpuri area, 7% of the villagers used this product (10).

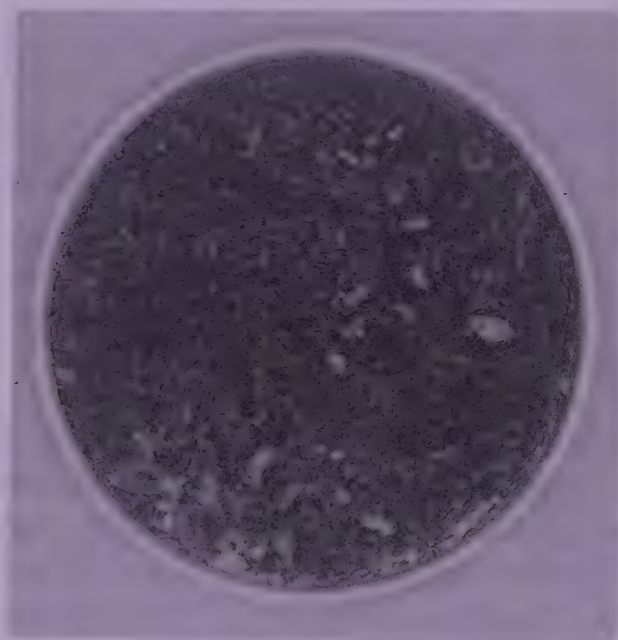


Fig. 10. Mainpuri tobacco

**Mawa:** This is a preparation containing thin shavings of areca nut with the addition of some tobacco and slaked lime (26). Its use is becoming popular in Gujarat, especially among the young; the habit is also prevalent in other regions of the country.

**Mawa** is sold by vendors as a 10 cm<sup>2</sup> mass in cellophane. Some 5-6 g of areca-nut shavings are placed on the cellophane and about 0.3 g of tobacco are added; a few drops of watery slaked lime are sprinkled over this, and the contents are tied with a thread into a ball (Fig. 11). At the time of use, the packet is rubbed vigorously on the palm to homogenize the contents. It is then opened and a portion is taken in the palm. Unmixed tobacco veins, if

any, are removed, and the mixture is chewed until it becomes soft, after which it is transferred to the mandibular groove. *Mawa* is then sucked for 10-20 min, by which time it has



Fig. 11. Mawa preparation

become bland. Sometimes, only half of the *mawa* quid is chewed at once. A person may chew as many as 5-25 times a day.

Although the prevalence of this habit is not known exactly, its magnitude can be assessed from the fact that the Bhavnagar city administration appealed to people not to litter the streets with the cellophane wrappers of *mawa*, as they clogged the city drains!

**Tobacco and slaked lime (*khaini*):** Use of a mixture of sun-dried tobacco and slaked lime, known in some areas as *khaini*, is widespread in Maharashtra and several states of North India. A regular *khaini* user may carry a double-ended metal container, one side of which is filled with tobacco and the other with slightly moistened slaked lime. A small quantity of tobacco is taken in the palm, and a little slaked lime is added (Fig. 12). The ingredients are then mixed vigorously with the thumb to make them alkaline (pH 8.3) and placed in the mouth. In Maharashtra and Gujarat, *khaini* is placed in the premolar region of the mandibular groove, whereas in Bihar and Uttar Pradesh, it is generally held in the lower labial groove. In Singhbhum district, Bihar, this product is often kept on the dorsum of the tongue.



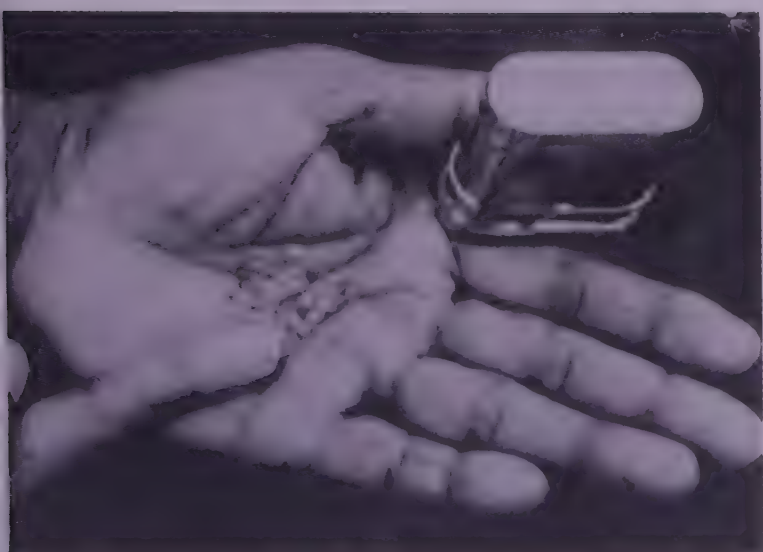


Fig. 12. Preparation of *khaini*

The average weight of this mixture for a single use is about 0.2 g (27). There is wide variation in the frequency of *khaini* use, ranging from 3 to 30 times per day. *Khaini* is generally not chewed as such but is retained in the location and sucked slowly for 10-15 min. Occasionally, it is left in the groove overnight.

In a study of over 100 000 villagers in Pune, Maharashtra, 28% used tobacco-lime (3); the habit was more common among men (52%) than women (10%). In Singhbhum and Darbhanga districts of Bihar, 27% and 44% of the 4800 and 4856 men used *khaini* and of the 5248 and 5481 women, 10% and 7% used *khaini* (Tables 4 and 5).

**Chewing tobacco:** Small pieces of raw or commercially available finely cut tobacco are used for this purpose. Chewing of tobacco alone, however, does not appear to be very common in India. Among 10 000 dental out-patients in Lucknow, Uttar Pradesh (1), and 57 000 industrial workers in Ahmedabad city in Gujarat (28), 2.1% and 2.6%, respectively, chewed tobacco alone. It does not appear to be popular in rural areas either (Tables 4 and 5).

**Tobacco products for application:** Several smokeless tobacco preparations, *mishri*, *gudhaku*, *bajjar* and creamy snuff, are intended primarily for cleaning teeth (Fig. 13). Such use, however, soon becomes an addiction.

*Mishri* is a roasted, powdered preparation made by baking tobacco on a hot metal plate until it is uniformly black. Women, who use it to clean their teeth initially, soon apply *mishri* several times a day (Fig. 14). Generally, it is carried in a small metal container; it is taken



Fig. 13. Tobacco preparations for application:  
(a) *mishri*; (b) *gudhaku*; (c) *bajjar*;  
(d) creamy snuff

out with the index finger and applied to teeth and gums. This habit is common in Maharashtra; in a survey of 100 000 individuals in this area, 22% were *mishri* users (3); the prevalence was 39% among women and 0.8% among men. *Mishri* use is also prevalent in Goa (see paper by Vaidya *et al.*, this volume).

*Bajjar* is a dry snuff used commonly by women in Gujarat on the teeth and gums. The material is carried in a small metal container, and a twig is dipped in to the snuff and used to apply it. In this area, 14% of 4844 women (Table 5) used *bajjar* (earlier reported (2) as *mishri*).



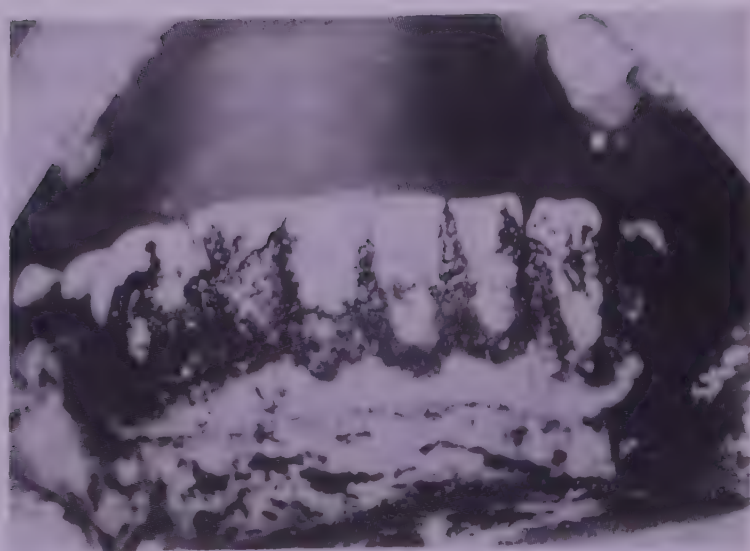


Fig. 14. *Mishri* applied to teeth

*Gudhaku* is a paste made of tobacco and molasses. It is available commercially and is carried in a metal container. *Gudhaku* is applied to the teeth and gums with a finger, predominantly by women. In Singhbhum district, Bihar, 1% of the men and 16% of the women used *gudhaku* (Tables 4 and 5); it is also used in other eastern regions of India.

*Creamy snuff*. Recently, commercial preparations of tobacco paste have been marketed in tubes like toothpaste. They are advertised as possessing antibacterial activity and being good for the gums and teeth. These products are thus used like a regular toothpaste; but users soon become addicted. This habit seems popular in children in Goa (see paper by Vaidya *et al.*, this volume).

### USE OF ARECA-NUT PREPARATIONS

Areca-nut chewing is an important etiological factor for oral submucous fibrosis (see paper by Sinor *et al.*, this volume). Some areca-nut preparations are chewed without the inclusion of tobacco (Fig. 15), but this practice may be present concurrently with use of smokeless tobacco or tobacco smoking. Areca-nut alkaloids are known to give rise to carcinogenic nitrosamines (23), which might have an additive effect when used with tobacco preparations (see paper by Hoffmann *et al.*, on smokeless tobacco, this volume). Therefore, a brief resume of these products is included.

*Areca nut*: Occasional chewing of areca nut (usually processed) alone is quite common in India, but habitual chewing is comparatively rare. Areca-nut chewing was observed among 0.2% of 57 000 industrial workers in Ahmedabad, Gujarat (29), and 2% of 100 000



Fig. 15. Areca-nut preparations: (a) raw areca nut; (b) sun-cured areca nut; (c) processed areca nut; (d) scented *supari*; (e) *pan masala* without tobacco; (f) betel quid without tobacco

villagers in Maharashtra (3); in other rural areas of India also, areca nut-chewing is practised to a limited extent (Tables 4 and 5).

In Assam, a fermented form of areca nut, known as *tamol* or *bura tamol*, is chewed extensively. This is prepared by preserving raw



areca nuts together with areca leaves in an underground pit with an inner lining of straw for four months (24). *Bura tamol* is often infected with fungus. This product contains very high levels of arecoline.

*Supari*: Areca nut is known as *supari* in many North Indian languages. Some commercial *supari* preparations are made by cutting dried areca nuts into bits and roasting them in fat to which flavouring and sweetening agents and condiments are added. *Supari* is marketed in attractive aluminium foil packs, in tins and in simple paper packets. Offering *supari* to guests, especially after meals, is a prevalent and well accepted social custom.

*Pan masala*: As described above, *pan masala* is available with and without tobacco. Suffice it to add here that *pan masala* without tobacco is also extremely popular.

*Meetha mawa*: *Meetha* (sweet) *mawa* consists of thin shavings of areca nut, grated coconut, dried fruits and other sweetening agents. It is used commonly in Gujarat, and similar preparations with different names are used widely in other regions.

*Pan without tobacco*: Occasional *pan* chewers generally prefer *pan* without tobacco. As described earlier, chewing *pan* without tobacco, known as *tambula* in Sanskrit, is a very ancient practice in India. Areca nut is an indispensable ingredient of *pan*.

## REASONS FOR USING TOBACCO

The reasons for initiating a tobacco habit vary from one geographical area to another. In a study of 10 000 individuals in Ernakulam district (Table 6), the two most important reasons given were tooth-related problems (48%),

**Table 6**

*Reasons for taking up tobacco habits in Ernakulam district, Kerala, India*

Reason	Men		Women		Total	
	No.	%	No.	%	No.	%
None	1114	15	81	3	1 195	11
Imitating elders	301	4	97	3	398	3
Peer-group influence	4001	53	70	2	4 071	38
Tooth-related problems	2159	28	3013	92	5 172	48
Total	7575		3261		10 836	

**Table 7**

*Distribution of tobacco users according to educational level*

Education	No habit (n = 262; 50%)		Smoking (n = 155; 30%)		Chewing (n = 78; 15%)		Mixed (n = 26; 5%)		Total (n = 521; 100%)
	No.	%	No.	%	No.	%	No.	%	No.
Illiterate	21	27	15	19	34	43	9	11	79
Primary or less	45	27	68	41	37	23	14	9	164
Middle school	59	57	37	35	5	5	3	3	104
High school	102	75	33	24	2	1	—	—	137
College	35	95	2	5	—	—	—	—	37

such as carious teeth and periodontal diseases, and peer-group influence (38%). Peer-group influence was the commonest reason among men (53%), whereas tooth-related problems were the single most important initiating factor for women (92%).

Use of tobacco was linked to educational level (Table 7): for instance, in a sample of 521 individuals selected from 5200 households, a high proportion of nonusers of tobacco (73%) were literate. In contrast, there was an increased proportion of tobacco users with decrease in educational level.

The reasons for continuing the habit may not be the same as those for initiating it. Once an individual acquires the habit, the addictive nature of tobacco plays the most important role in its continuation.

### DYNAMICS OF TOBACCO USE

The tobacco use behaviour of individuals may change over a period of time. Two 10-year prospective studies — one in three districts (30) and another among Bombay policemen (31) — provided some long-term observations on the dynamics of tobacco use. In a population-based study (30) of 30 000 individuals (Table 8), the habit remained constant in 47-73%, and 3-5% of those with no tobacco

habit started tobacco use over the 10-year period; a similar proportion gave up tobacco use on the basis of the advice of dentists. In 13-34%, the habit was inconsistent, so that some gave up, re-started and gave up the habit again.

In the study of 3674 Bombay policemen, there were 846 nonusers of tobacco (31). After 10 years of observation 434 nonusers acquired some kind of tobacco habit; 55% acquired chewing habit, 29% started cigarette smoking and 7% became *bidi* smokers. Furthermore, many of those who practised only smoking or chewing habits initially acquired chewing or smoking habits subsequently. Only 4% of those who smoked and chewed gave up these habits.

### HEALTH CONSEQUENCES OF TOBACCO USE

A causal relationship between tobacco use and both oral cancer and precancerous lesions is well accepted. Tobacco use is also linked with cancers of the upper aerodigestive tract and other diseases of the heart and respiratory tract.

Annually, more than 630 000 deaths in India are attributable to tobacco use (32), as estimated from mortality rates attributable to

Table 8

*Tobacco habits over a 10-year period in three areas of India<sup>a</sup>*

Tobacco habits	Ernakulam		Srikakulam		Bhavnagar	
	No.	%	No.	%	No.	%
Constant	4026	73	4757	69	1359	47
Acquired	284	5	240	3	78	3
Discontinued	179	3	218	3	121	4
Changed	304	6	258	4	344	12
Inconstant	712	13	1459	21	996	34
Total	5505		6932		2898	

<sup>a</sup>Source: ref. (30)



specific forms of tobacco use. In Ernakulam, the age-adjusted relative risks for overall mortality associated with tobacco chewing and smoking were 1.3 for women and 1.5 for men, respectively (33). These rates, which are highly significant, cannot be explained by oral cancer alone. In Srikakulam, the age-adjusted relative risk for mortality among reverse smokers compared to nonusers of tobacco was significantly high (1.95) for men and 1.91 for women, respectively (34). In Maharashtra, the crude annual mortality rates among *bidi* smokers and among chewers were 45 per 1000

and 28 per 1000, respectively (35), indicating that, like cigarette smokers, *bidi* smokers also have high overall mortality rates. The specific health consequences of tobacco use are described in detail in other papers in this volume.

### Acknowledgments

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# Challenges in tobacco control in India: a historical perspective

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The major economic and other challenges to tobacco control in India are put into a historical perspective. Over the century after the introduction of tobacco into the country in the early 17th century, the common indigenous products, such as *hookah*, *chutta*, *bidi* and tobacco chewing, were innovated. The area under tobacco cultivation grew rapidly from 1880, until it stabilized at around 450 000 ha in 1970; subsequent increases are due primarily to improvements in yield. Cigarette and *bidi* smoking and tobacco chewing are the major forms of tobacco use in India. Tobacco cultivation, manufacture and distribution provide employment to millions of people. A sizable proportion of the central excise revenue from tobacco is generated by cigarette consumers; *bidi*, *hookah*, *chutta* and chewing tobacco yield very little tobacco revenue as they are consumed largely by poor people. Public information and education on tobacco should be implemented immediately to control tobacco use. Concurrent strategies to curb tobacco use might take the form of enhancing taxation, and extending it to indigenous tobacco products, curbing advertisements for cigarettes and *bidis*, and reducing tar and nicotine levels of all products. Tobacco should eventually be substituted by other crops and tobacco-related employment transferred to other occupations.

## INTRODUCTION

India is the third largest producer of tobacco after China and the USA. Although the *per-caput* consumption of tobacco in India is relatively low, the manner in which it is consumed increases the health hazards considerably. For instance, every gram of tobacco is used to produce about one cigarette but three to four *bidis*. Similarly, for every cigarette smoker, there are four to five *bidi* smokers in the country. *Bidis* and Indian-made cigarettes deliver far more toxic products to the smoker than US brands of cigarettes (see paper by Bhonsle *et al.*, this volume).

The problem of tobacco-related cancers and other diseases is as serious in India as in western countries, although it is of a somewhat different nature. In a UICC workshop held in Bombay in 1987, the available scientific evidence on the burden of tobacco-related

diseases and deaths was evaluated critically. It was estimated that over 630 000 deaths per year could be attributed to the use of tobacco (1). The workshop also considered short-term and long-term measures to reach the goal of a non-tobacco-using generation. This paper focuses on some of the major challenges in tobacco control in a historical perspective.

## EARLY HISTORY OF TOBACCO IN INDIA

Soon after the introduction of tobacco into India in the late 16th or early 17th century, it became a valuable commodity in barter trade and spread rapidly along the Portuguese trade routes in the east, *via* Africa to India, Malaysia, Japan and China. Cochin and Goa on the west coast and Machilipatnam on the east coast of India were the important ports for Portuguese trade (2).



Early use of tobacco in India and in Europe was in pipes 5-6 feet long. Tobacco was a luxury item in the glittering city of Bijapur in peninsular India; its entry to the Moghul court of Emperor Akbar in the north and the creation of *hookah* (3) are described elsewhere (see paper by Bhonsle *et al.*, this volume). As the popularity of tobacco grew, it began to be grown in abundance in India, and by the middle of the 17th century it was exported to many ports along the Red Sea.

The habit of smoking a rolled tobacco leaf preparation known as *chutta* was noted on the east coast of India as early as 1670. Another account of smoking, in 1711, describes a product about the size of the little finger containing a small quantity of tobacco wrapped in the leaf of a tree and sold in bundles of 20-30 pieces. This description corresponds to the present-day *bidi* (see paper by Bhonsle *et al.*, this volume). Tobacco was chewed by itself, with areca nut or with lime in India as early as 1708. Tobacco was generally used to stave off hunger during travel and to sustain long hours of tedious work. This brief account shows that the tobacco habits that are currently popular in India had modest beginnings in the 17th century.

The growth of tobacco cultivation, the development of different tobacco products and the tobacco trade are intimately linked with the history of the British East India Company, which used tobacco as an important cash crop to generate farm revenue and foreign trade. Quantitative information on these issues is also available for the period after the East India Company and its colonial possessions were taken over by the Crown in 1858. The following section summarizes this information.

## TOBACCO CULTIVATION AND TRADE

**British India:** Statistical abstracts on British India published periodically since 1881 are a valuable source of information on tobacco

cultivation and trade. Two volumes, one covering the period 1882-83 to 1891-92 and the other from 1912-13 to 1921-22 (4,5), have been the source of data for this paper. These two volumes cover information on (i) the total area under tobacco cultivation in British India, (ii) the areas under cultivation in different regions (presidencies) and (iii) foreign trade in tobacco, including the quantities of tobacco exported and imported.

The areas under tobacco cultivation in different regions of British India, a comparison of the data for 1891-92 with the corresponding figures for 1920-21, and the trends during the three decades are given in Table 1. Unfortunately, for the Bengal presidency, which had the largest area under tobacco cultivation in 1920-21, there was no information for the period 1891-92; so this area was excluded from the analysis. The area under tobacco cultivation in the rest of India nearly tripled over this period. Tobacco cultivation was fairly common all over the country, particularly where the East India Company had settlements. In the subsequent three decades, tobacco

**Table 1**

*Area under tobacco cultivation ( $\times 10^3$  ha) in British India: 1891-92 and 1920-21*

Area	1891-92	1920-21	% Change
Bengal	Not available	120.6	—
Bihar	8.2	47.9	584
Madras	29.4	82.2	280
Bombay	34.9	48.6	139
Oudh	4.6	36.2	787
Punjab	17.6	36.4	207
Burma	16.8	34.9	208
NWFP	12.1	3.6	-70
Others	8.7	14.7	169
Total	132.3	425.1	



cultivation spread to other regions covering more than 400 000 ha.

Information on foreign trade in tobacco is given in Tables 2 and 3. The revenue from tobacco exports increased from about Rs. 1 million in 1881-82 to about Rs. 7 million in 1921-22 (Table 2). There was a considerable increase in tobacco imports, mostly of manufactured cigarettes, during the same period. These imports were worth less than Rs. 1 million in 1881-82 but had risen to Rs. 25 million by 1920-21. At this time, cigarette factories were established in India; consequently, the imports declined from then onwards.

**Table 2**

*Tobacco trade in British India: 1881-82 to 1921-22*

Years	Exports (million Rs.)	Imports (million Rs.)
1881-82	1.197	0.632
1891-92	1.414	1.671
1912-13	3.836	6.939
1920-21	7.492	25.591
1921-22	7.131	16.506

The quantity of raw tobacco exported from India and the price that it fetched is given in Table 3. This table also shows the quantity of manufactured tobacco that was imported and the price paid. Raw tobacco exported from

**Table 3**

*Tobacco trade in British India: ratio of import and export prices, 1912-13 to 1921-22*

Years	Exports		Imports		Ratio of prices
	$\times 10^3$ tonnes	Price (Rs./kg)	$\times 10^3$ tonnes	Price (Rs./kg)	
1912-13	9.940	0.39	1.067	6.50	16.7
1920-21	11.197	0.67	3.451	8.57	12.8
1921-22	10.990	0.65	1.843	8.96	13.8

India fetched Rs. 0.4 per kg prior to the First World War, and the price increased to Rs. 0.7 after the War. The price of imported manufactured tobacco declined from Rs. 17 per kg before the War to about Rs. 14 per kg afterwards. There was a substantial decline in the imports of manufactured tobacco in 1921-22 compared to 1920-21; there was, however, very little change in tobacco exports during that period.

The data on world tobacco production in 1938, just prior to the Second World War, and the relative positions of tobacco-producing countries (6) are given in Table 4. Total world production of tobacco was about 2.8 million tonnes. Production in British India came next to that of the USA and was slightly higher than that in China; the USSR and Brazil ranked fourth and fifth, respectively.

**Table 4**

*World tobacco production, 1938*

Country	Production ( $\times 10^3$ tonnes)
USA	628.7
British India	499.0
China	446.8
USSR	270.3
Brazil	95.1
Total	2797.3

World tobacco production, areas under tobacco cultivation, total weight of tobacco produced and yields in kg/ha in the following decades are given (7-9) in Table 5. The table also gives details for the major tobacco-producing countries for 1983-84. Total world tobacco production nearly doubled during the four decades, from 2.8 million tonnes in 1938 (Table 4) to about 6 million tonnes in 1983-84. China became a major producer of tobacco both in terms of area under cultivation and productivity. The area known as British India



**Table 5***World tobacco — area and production: 1960-64 to 1983-84*

Years	Area ( $\times 10^3$ ha)	Production ( $\times 10^3$ tonnes)	Productivity (kg/ha)
1960-64	3761.5	4038.3	1074
1970-74	4055.3	4734.1	1167
1983-84	4078.0	5920.1	1452

Major tobacco producing countries (1983-84)

China	748.0	1400.0	1872
USA	321.9	746.0	2317
(British India <sup>a</sup> )	(586.4)	(645.1)	(1100)
India	440.1	497.1	1130
Brazil	273.0	373.0	1366
Turkey	208.0	210.0	1010

<sup>a</sup>Now Indian subcontinent: figures for 1981

in 1938, presently comprising Pakistan, Bangladesh, Sri Lanka and Burma, ranked third in world tobacco production. Although this region had a substantial area under tobacco cultivation, the productivity was poor. Production of tobacco in India was similar to that in other countries in the region. Brazil improved its rank to fourth, with a considerable increase in productivity, and Turkey replaced USSR in the fifth rank.

**Tobacco scene since 1950:** Comparative data on tobacco production in India from 1950-51 to 1980-81 are given in Table 6. Production increased during the first two decades, largely owing to the putting of a larger area under tobacco cultivation and, to a limited extent, to an improvement of productivity. During the last decade, however, this trend reversed: the yield improved from 810 kg/ha to 1065 kg/ha during the period 1970-71 to 1980-81, whereas the area under tobacco cultivation changed very little.

**Table 6***Production of tobacco in India, 1950-51 to 1980-81*

Years	Area ( $\times 10^3$ ha)	Production ( $\times 10^3$ tonnes)	Yield (kg/ha)
1950-51	357.3	261.1	731
1960-61	401.0	307.0	766
1970-71	446.9	361.9	810
1980-81	451.5	480.8	1065

**Table 7***Area under tobacco cultivation ( $ha \times 10^3$ ) in different states, 1960-61, 1970-71 and 1980-81*

State	1960-61	1970-71	1980-81
Andhra Pradesh	143.0	222.1	169.4
Gujarat	93.0	46.9	121.5
Karnataka	39.0	42.5	51.6
Maharashtra	26.0	13.2	11.9
Bihar	16.0	13.5	12.5
Tamil Nadu	19.0	14.6	14.5
Uttar Pradesh	19.0	10.9	15.4
West Bengal	17.0	10.1	18.9
Orissa	—	—	21.2
Total, including other states	401.0	446.9	451.5

Comparative data on the area under tobacco cultivation in different states of India from 1960-61 to 1980-81 are given in Table 7. Andhra Pradesh, Gujarat and Karnataka had relatively large areas under tobacco cultivation, accounting for over 70% of the tobacco produced in the country, although the hectareage fluctuated widely during different periods. For instance, there was a considerable increase in Andhra Pradesh in 1970-71, while Gujarat showed a decline. Furthermore, most cigarette tobacco is produced in Andhra Pradesh, whereas Gujarat and Karnataka produce most of the *bidi* tobacco.



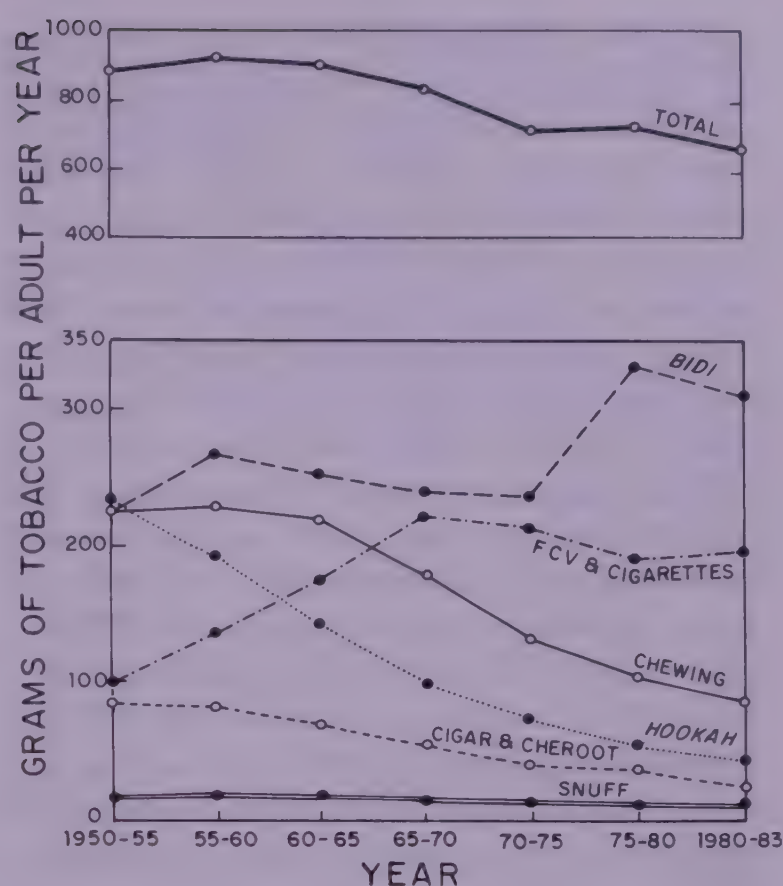
Marked variations in productivity were seen in different states in 1983-84 (Table 8). The highest yield (1726 kg/ha) was that in Gujarat, whereas in Orissa and Karnataka the yields were very low (548 and 600 kg/ha, respectively). A relatively large production of *bidi* tobacco seen in Gujarat is due to a large area under cultivation and high productivity.

Although there was a continuous increase in tobacco production in the country during the three decades under consideration, it must be realized that the population increase during this period was faster. This resulted in a decline in the per adult consumption of tobacco from about 900 g during the period 1950-60 to less than 700 g in the period 1980-83 (Fig. 1). Furthermore, there was a major change in the pattern of consumption of different tobacco products during this period. For example, consumption of *bidi* and cigarette tobacco increased, whereas that of tobacco used for chewing, *hookah* smoking and other purposes declined.

**Table 8**

*Area, production and productivity of tobacco in different states (1983-84)*

State	Area ( $\times 10^3$ ha)	Production ( $\times 10^3$ tonnes)	Productivity (kg/ha)
Andhra Pradesh	187.1	191.9	1026
Gujarat	108.3	186.9	1726
Karnataka	48.0	28.8	600
Maharashtra	10.1	7.9	728
Bihar	13.4	13.4	1000
Tamil Nadu	12.4	13.7	1150
Uttar Pradesh	14.7	19.7	1340
West Bengal	15.4	15.5	1026
Orissa	18.6	10.2	548
Others	12.4	9.8	790
Total	440.1	497.1	1130



*Fig. 1. Total tobacco consumption in grams per adult per year according to types of tobacco use in India, 1950-55 to 1980-83 F.C.V., Flue-cured Virginia*

Reliable data on tobacco use patterns in the country are not available for recent years but can be estimated on the basis of limited surveys and from data on tobacco consumption (Fig. 1). The results of this reconstruction are given in Table 9, which shows the estimated number (in millions) of people aged 15 years and over who smoked *bidi* or cigarettes or chewed tobacco. Other tobacco habits, the prevalence of which has declined in recent

**Table 9**

*Estimated number of people (in millions) aged 15 years and over in India with different tobacco habits, 1950-55 to 1980-83*

Tobacco habit	1950-55	1965-70	1980-83
Cigarette smoker	6	18	22
<i>Bidi</i> smoker	58	79	136
Tobacco chewer	47	49	31
Total population	230	300	400



years, have not been taken into account. No attempt has been made to separate the genders for this analysis, although it is known that such habits are quite different among men and women. Most *bidi* and cigarette smokers, for example, are men, whereas tobacco chewing habits are equally common in men and women. Cigarette smoking is much less common than *bidi* smoking and tobacco chewing; however, the two latter habits were common in 1950-55 and changed their course during the following three decades: *bidi* smoking became predominant in the population, whereas tobacco chewing declined considerably in the latter period. In the absence of reliable national data on tobacco habits, the present reconstruction provides only a broad assessment of the common habits in the country, and it is presented here merely to serve as a guideline for action.

Data on cigarette production are available from 1950 onwards (Table 10). These show a continuous increase in production over the

**Table 10**

*Estimated annual output and per-adult consumption of cigarettes in India, 1950-54 to 1985-86*

Period	Average annual output (billions)	Annual per-adult consumption
1950-54	25.0	111
1955-58	27.8	115
1960-64	40.8	155
1965-69	57.4	198
1970-74	63.2	193
1975-79 <sup>a</sup>	69.0	184
1980-84	85.1	200
1985-86	76.7 <sup>b</sup>	162 <sup>c</sup>
1987 <sup>d</sup>	62.0	—

<sup>a</sup>Cigarette Act, 1975

<sup>b</sup>Average of 80.7 and 72.7 for 1985 and 1986

<sup>c</sup>Changes in cigarette taxation procedures

<sup>d</sup>Provisional

last three decades, although the per-adult consumption has remained stationary at around 200 cigarettes. Since 1985, there has been some indication of a decline in cigarette consumption, but it is not clear whether it is a definite trend. Such figures are not available for *bidi* and other tobacco products, which are manufactured in the unorganized sector of industry and contribute substantially to health hazards, especially among the poorer sections of the population.

## TOBACCO ECONOMICS

There is a strong need to develop a comprehensive assessment of tobacco economics in the country. Such an exercise should include information on tobacco cultivation, number of farm hands involved in the cultivation of different types of tobacco, numbers of people engaged in curing and processing tobacco and income of various categories of personnel; some of this information was already given earlier in this paper. Tobacco cultivation is labour-intensive and requires experience and special skills. It is estimated that about 1 200 000 people are engaged in the cultivation of tobacco, its curing and processing.

Cigarette manufacture is a capital-intensive industry in the organized sector, employing a limited labour force. There are 20 cigarette factories in the country; some of the larger manufacturers have begun to diversify into other sectors, perhaps anticipating a fall in cigarette sales. *Bidi* and other tobacco products are manufactured in the unorganized sector and therefore come under the control of respective state governments. The *bidi* industry is a highly labour-intensive cottage industry and provides part-time and full-time employment to more than three million people. Collection of *tendu* leaf, which is used as the wrapper for *bidi*, provides part-time employment to hundreds of thousands of tribal people. Trade and distribution of cigarettes, *bidis*, chewing tobacco and other tobacco products provide employment to over 500 000 people.



Economic sample surveys carried out periodically (10) by the Planning Commission provide information on total expenditure for private consumption under several headings, including tobacco. Data available for 1980-81 show (Table 11) that 2.3% of total household expenditure was on tobacco, which accounted for more than Rs. 20 000 million out of a total of about Rs. 900 000 million incurred for household expenditure in 1980-81.

**Table 11***Private consumption expenditure, 1980-81*

Item of expenditure	Total expenditure (Rs. millions)	Per-caput (Rs.)	% of total expenditure
Food			
<i>Pan</i> , alcohol and tobacco	33 850	50 <sup>a</sup>	3.8
Tobacco	20 300	30	2.3
Other	13 550	20	1.5
Other food items	509 720	752	56.9
Clothing, household and transport	261 060	386	29.1
Education and health	52 720	77	5.9
Miscellaneous	38 470	57	4.3
Total	895 820	1322	100.0

<sup>a</sup>*Per-caput* expenditure on this item declined at a compound rate of 0.8% between 1960-61 and 1980-81 at 1970-71 prices

Data are also available on central excise revenue from tobacco and tobacco products for 1950-51 to 1980-81 (Table 12). The data for cigarette, *bidi* and chewing tobacco are given separately, as these continue to be the predominant habits. Cigarettes are a major source of central excise revenue; currently, the excise revenue from cigarettes may be more than Rs. 15 000 million a year. *Bidis*, which have a larger turnover than cigarettes, contribute a much smaller amount to the

central exchequer; other tobacco products contribute even smaller amounts by way of tobacco revenue.

**Table 12***Central excise revenue (Rs. million) from tobacco and tobacco products, 1950-51 to 1980-81*

Product	1950-51	1960-61	1970-71	1980-81
Cigarette	13.0	263.5	1709.8	6133.9
<i>Bidi</i>	7.8	143.4	231.2	1195.7
Chewing tobacco	3.4	63.8	92.0	166.2
Other products	5.8	114.2	227.8	57.6
Total	30.0	584.9	2260.8	7553.4

Tobacco was considered to be a major cash crop for export and received considerable governmental support in the mid-1970s. The introduction of Virginia tobacco, which carried a premium price on the international market, initiated a major shift in the area of cultivation from black to light soil. The export earnings, which rose rapidly from Rs. 314 million in 1970-71 to Rs. 1244 million in 1980-81 (Table 13), were reported to have risen to Rs. 2000 million in the mid-1980s. Since then, they have started declining because of competition and the fall in demand.

An exercise to estimate the total cost of tobacco-related diseases to the central and state governments, voluntary agencies and households was undertaken by the Indian

**Table 13***Export revenue (Rs. millions) from tobacco and tobacco products, 1950-51 to 1980-81*

Type of tobacco	1950-51	1960-61	1970-71	1980-81
Unmanufactured	130.5	146.1	314.0	1244.1
Manufactured	21.6	11.3	11.6	162.7
Total	152.1	157.4	325.6	1406.8



Council of Medical Research (see paper by Luthra *et al.*, this volume).

These aspects of tobacco economics are of vital importance for policy issues for tobacco control and require careful compilation of current data and a comprehensive assessment.

## STRATEGIES FOR TOBACCO CONTROL

Tobacco control strategies should start with a programme on public awareness, which should include detailed information about the health hazards of tobacco, followed by public education at different levels. Such a programme should motivate people to give up their tobacco habits and should prevent nonusers of tobacco, especially vulnerable children and adolescents, from starting to use it. There are, however, limitations to such an approach in India, where massive health and family welfare educational programmes have yet to achieve their desired objectives. The national family planning programme, initiated in 1950 with substantial input, has achieved only limited success after four decades of intensive effort. Similar observations can be made with regard to other health education programmes, such as immunization of infants and children and eradication of leprosy and tuberculosis.

In western countries, reduction of the tar and nicotine levels in cigarettes has been widely accepted by both cigarette manufacturers and consumers over the last two to three decades. This has resulted in considerable reduction in the tar and nicotine levels to which those populations are exposed. There is a reasonable chance of success for such an approach in India. Cigarette manufacturers who are currently marketing relatively high tar-high nicotine cigarettes are fully geared for such a change, and a little governmental action in this direction would have a positive effect. Similar measures can be adopted to reduce the toxicity of *bidis*: adequate information on cheap, effective filters for *bidi*, which are acceptable to the users, already exists, based

on scientific work carried out in the country. Initially, *bidi* manufacturers showed some interest in this approach when they were shown that *bidis* deliver as much tar and nicotine and much more carbon monoxide compared to Indian cigarettes. However, a total lack of interest from the central and state governments meant that the manufacturers did not adopt this novel method for making *bidis* less hazardous, and, in fact, they diverted their attention and resources to exerting political pressure to thwart any purposeful action on *bidi*.

The tobacco tax is a vital source of funds for governments. In recent years, it has also been shown to be a powerful instrument for counteracting cigarette sales and bringing about behavioural modification among smokers in industrialized countries. This is also true for India, where increased taxation on cigarettes during the last few years has had a significant impact in terms of reducing the per-adult consumption of cigarettes. It has also further enhanced the central excise revenue. This area should be pursued with vigour. However, governments often refrain from increasing taxes on tobacco products, and especially *bidi* and other preparations, because they are more often used by poor people. This is ironic, because *bidi* smoking damages the health of poor people much more than cigarette smoking affects the affluent classes. There is, therefore, an urgent need for anti-tobacco groups to urge positive action by government on these issues and thus save the poor from major, preventable health hazards.

Although there are some inherent problems (see paper by Chari and Rao, this volume), the solution in the long run is to develop alternative uses of tobacco and alternative crops (preferably food crops) to be planted in place of tobacco. The promising work carried out by the Indian Council of Agriculture Research in this direction should be pursued with vigour. A similar approach is essential in forestry research to find suitable alternative uses for *tendu* leaves.



All these strategies should be initiated concurrently. In order to do so, the central and state governments, which share substantial

tobacco excise revenue, should set apart a reasonable fund for conducting anti-tobacco activities.

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# Role of tobacco in the national economy: past and present

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The two species of the genus *Nicotiana* that are cultivated extensively are *tabacum* and *rustica*. Different types of *N. tabacum* are used for making cigarettes, cigars, cheroots, *bidis*, *hookah* and snuff tobacco, while those of *N. rustica* are used for chewing, and as *hookah* and snuff tobacco. Some tobacco by-products find use in the pharmaceutical industry and as pesticides. Millions of people depend on tobacco-related activities for their livelihood, and tobacco earns vast sums as revenue and in foreign exchange. Most tobacco is grown in southern and western India. Farmers grow tobacco because it is remunerative, drought tolerant and easy to grow, while substitute crops like cotton, chillies, chickpeas, mustard and coriander are either not remunerative or are susceptible to pests. Although tobacco use is harmful to health, it would be impracticable to eradicate or drastically limit its availability. Measures that could be used to mitigate the health hazards of tobacco are: making tobacco less hazardous by blend modification, introducing effective filters and improving filter ventilation and paper porosity to dilute the smoke. Other avenues that should be explored are economically viable, tobacco-based cropping systems, the potential of tobacco as an oil-seed crop and alternative uses.

## INTRODUCTION

The generic name of the tobacco plant, *Nicotiana*, and the word nicotine are derived from the name of the French ambassador to Portugal, Jean Nicot, who came to know of tobacco in Lisbon and introduced it into the French court in 1560. Tobacco is considered to be native to South America. *Nicotiana* is one of the five large genera of Solanaceae and is represented by 68 recognized species, of which only two, *tabacum* and *rustica* are cultivated extensively.

A detailed account of the origin, history and introduction of tobacco into India are described elsewhere (see papers by Bhonsle *et al.*; Sanghvi, this volume).

## TOBACCO CULTIVATION IN INDIA

India grows both species, but the largest area is under *N. tabacum*, and cultivation of *N. rustica*

is confined mainly to northern, north-eastern and western India. Specific varieties of *N. tabacum* have been developed for cigarette, cigar, cheroot, *bidi*, *hookah* and snuff tobaccos; while varieties of *N. rustica* are used for chewing and as *hookah* and snuff tobacco. All these types of tobacco are grown in India (Fig. 1). The largest quantities of tobacco are consumed for smoking, chewing and snuff; while very small quantities of tobacco waste are used in the manufacture of nicotine sulfate, used as an insecticide.

Flue-cured virginia tobacco (cigarette tobacco) was introduced into India by the M/S Imperial Tobacco Company, Indian Leaf Tobacco Division, in Guntur, Andhra Pradesh, in 1929. It was cultivated in black soils after cessation of the rains to produce a lustrous leaf with a lemon-yellow/orange colour. Medium-bodied with a moderate aroma, it was found suitable for cigarette blending



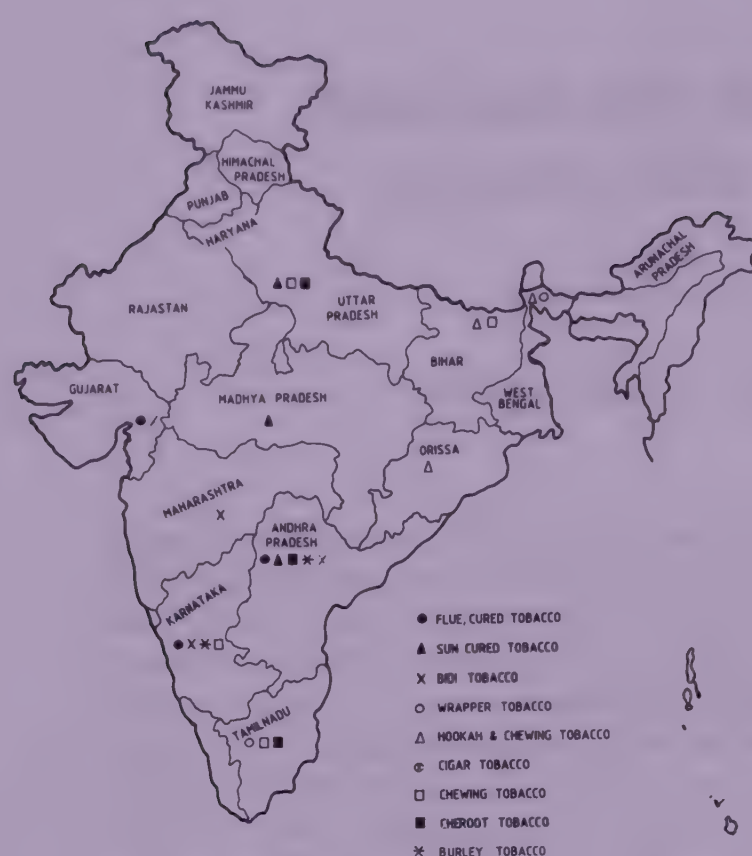


Fig. 1. Tobacco map of India

purposes. In 1934, the Central Government enacted the Central Excise Act, giving the Central Excise Department full control over the cultivation and movement of this crop.

Cultivation of tobacco began to increase in the 1940s; a cigarette tobacco research station was established at Guntur in Andhra Pradesh in 1938 in order to improve the yield and quality of tobacco. The area under tobacco was extended to Krishna and Godavari districts in Andhra Pradesh, and by 1945 about 20 000 ha were under cultivation. To improve tobacco cultivation and marketing, in 1945, the Government of India constituted the Indian Central Tobacco Committee, which included growers, traders, manufactures, scientists and cigarette consumers as members. The Committee established the Central Tobacco Research Institute at Rajahmundry in 1947, which was brought under the aegis of the Indian Council of Agricultural Research in 1965.

Up to the 1960s, tobacco cultivation was confined mainly to black soils, but the shift in

the quality requirements of the overseas market, to preference for ripe fluffy tobaccos with good flavour, stimulated extension of cultivation to light soils. The light soils in Prakasam and Nellore districts of Andhra Pradesh and the transitional zone in the State of Karnataka, where the climatic conditions are favourable for cultivation of natural tobacco, were identified. Cultivation of tobacco in light soils was encouraged under centrally sponsored schemes of the Government of India, according to the recommendations of the Tobacco Development Council, which was set up in 1966. With the trend in favour of light-soil tobacco, the Tobacco Development Council introduced programmes to produce more exportable tobacco. In 1965, the light soils in West Godavari district were also identified for cultivation of irrigated flue-cured Virginia (FCV) tobacco, and experiments were conducted by the Indian Leaf Tobacco Division of the Imperial Tobacco Company. As there was high demand for light-soil tobacco, cultivation was rapidly extended to larger areas, particularly in the State of Karnataka and in East and West Godavari districts of Andhra Pradesh; by 1976-77, about 40% of tobacco was grown on light soils. FCV tobacco was also introduced in other states, like Gujarat, Uttar Pradesh, West Bengal and Tamil Nadu, but was later abandoned due to unsuitability. The areas and production of all tobaccos and of FCV tobacco in India between 1980-81 and 1988-89 are presented in Table 1.

## ECONOMIC IMPORTANCE OF TOBACCO PRODUCTION IN INDIA

Tobacco is one of the most important cash crops in India, and it is cultivated on an area of over 400 000 ha. It represents 0.3% of the total area under cultivation in India. Annual production of various types of tobacco is about 490 million kg. Indian tobacco represent about 10.4% of the world area under tobacco cultivation, 7.6% of world production and 6% of world export trade. Tobacco earns the



**Table 1**  
*Area and production of tobaccos in India<sup>a</sup>*

Year	All tobacco		Virginia tobacco			Bidi tobacco		
	Area ( $\times 10^3$ ha)	Production ( $10^3$ tonnes)	Area ( $\times 10^3$ ha)	Production ( $10^3$ tonnes)	Productivity (kg/ha)	Area ( $\times 10^3$ ha)	Production ( $10^3$ tonnes)	Productivity (kg/ha)
1980-81	452	491	149	117	787	140	175	1250
1981-82	444	520	160	151	944	130	190	1462
1982-83	503	582	197	173	879	125	180	1436
1983-84	440	492	138	117	848	126	176	1393
1984-85	437	486	123	107	869	126	175	1389
1985-86	397	441	116	98	882	128	172	1362
1986-87	389	462	105	114	1081	130	191	1458
1987-88	324	359	68	59	868	—	—	—
1988-89	—	—	96	116	1205	—	—	—

<sup>a</sup>Source: Tobacco Board, Guntur

—, not available

exchequer about Rs. 16 000 million (US\$ 928 million) in excise and Rs. 1720 million (US\$ 100 million) in foreign exchange. Human dependence on this crop from the point of view of employment is substantial: as many as 1 200 000 growers and curers are engaged in its production, and the cigarette industry, comprising 20 factories distributed all over India, provides employment to about 20 000 people.

Of the different types of indigenous tobacco grown in India, *bidi* tobacco ranks first. The principal areas in which this type of tobacco is grown are Gujarat (Kheda, Vadodara and Panchmahal districts), Karnataka (Nipani area of Belgaum district) and Maharashtra (Kolhapur and Sangli districts). Gujarat contributes more than 80% of the total from an area of about 90 000 ha. The *bidi* industry is one of the foremost cottage industries in India, employing about three million individuals; annual production is about 1500 million *bidis*. In some states, *bidi* production is the second largest employer after agriculture. During the 1980s, the industry's total turnover was estimated to be

Rs. 25 000-30 000 million (US\$ 1449-1739 million). Annual wages account for about Rs. 7000 million (US\$ 406 million), and excise revenue earned by the government was about Rs. 2000 million (US\$ 116 million).

Other sectors of the industry include the manufacture of chewing, cigar, cheroot and snuff tobacco and the packing, processing and exporting of tobacco; these involve several thousands of people. Transport agencies, like the railways, roadways and shipping, benefit immensely from the tobacco trade.

It is clear that tobacco production cannot be substituted or replaced immediately, as this industry employs hundreds of thousands of men and women and involves huge investments, particularly in the cigarette industry. It would, however, be possible to regulate production, to minimize the demands of the domestic market and to attract the export market by producing high-quality tobacco. The Tobacco Board is presently dealing with the problem of implementing production regulations to meet the requirements of domestic and international trade and to avoid excess production.

**Table 2**  
*Area and production of flue-cured Virginia tobacco in three states in India<sup>a</sup>*

Year	Area ( $\times 10^3$ ha)			Production ( $10^3$ tonnes)		
	Andhra Pradesh	Karnataka	Maharashtra	Andhra Pradesh	Karnataka	Maharashtra
1980-81	126	23	—	101	16	—
1981-82	141	19	—	128	23	—
1982-83	176	21	0.33	150	23	0.20
1983-84	115	22	0.34	94	23	0.20
1984-85	103	20	0.19	90	17	0.12
1985-86	98	18	0.22	80	18	0.20
1986-87	88	17	0.29	97	16	0.20
1987-88	52	16	0.20	47	12	0.20
1988-89	81	15	0.31	105	11	0.40

<sup>a</sup>Source: Tobacco Board, Guntur  
—, not available

**Table 3**  
*Economics of alternative crops to flue-cured Virginia (FCV) tobacco, 1989*

Crop	Yield (kg/ha)	Cost of cultivation (Rs./ha)	Gross income (Rs./ha)	Cost-benefit ratio
Safflower	1800	3661	14 400	1:4.0
<i>Manjira</i> (or)				
<i>Annagiri</i>				
Mustard	1500	3196	12 000	1:3.25
<i>Kranthi</i> (or)				
<i>Krishna</i>				
FCV Tobacco	1417	8464	17 620	1:2.0

Table 2 shows the cultivated area and production of FCV tobacco in three states. The area and production of FCV tobacco are on the decline, particularly since the 1982-83 season, due to regulatory measures imposed by the Tobacco Board as a result of lower demand in overseas markets. This trend is most conspicuous in Andhra Pradesh. Tobacco is a very remunerative cash crop for tobacco farmers, who are accustomed to cultivating this drought-tolerant crop and obtaining reasonable yields. Substitute crops, like cotton and

chillies, are not as remunerative as tobacco in Andhra Pradesh and Gujarat; furthermore, cotton is susceptible to many insect pests, and yields are very low. Chickpea, mustard, coriander and safflower have proved successful in the black soils of Andhra Pradesh, where FCV tobacco is grown traditionally; but these crops are subject to erratic market prices, and farmers may not wish to take the risks in view of the good economic returns from tobacco and their traditional long association with this crop (Table 3).



A comparison of the net yield of substitute crops under middle Gujarat conditions revealed that irrigated castor and cotton were more remunerative, with net realizations of Rs. 9702 (US\$ 562) and Rs. 9560 (US\$ 555), respectively. However, the requirements for nonedible oils at the national level and possible changes in the ecosystem due to heavy use of pesticides on cotton crops, including occupational health problems, must be examined critically before these crops can be suggested as possible substitutes in the existing tobacco growing area in Gujarat state.

More or less similar situations exist in Karnataka and in Andhra Pradesh; no substitute crop gave better income than FCV tobacco. In West Bengal, crops like potato, cauliflower and mustard are more remunerative than cigar filler and chewing tobacco, but due to overproduction of cauliflower and potatoes in some seasons, the farmers have to sell these produce at a low price and incur monetary losses. In Tamil Nadu, chewing tobacco is grown on 12 000-15 000 ha, and *bajra*, *ragi* and sorghum are cultivated as preceding and succeeding crops. Chillies, safflower, groundnut and cotton have been tried as substitute crops for chewing tobacco, but due to the erratic monsoon pattern in this area, farmers prefer to grow tobacco. In Bihar, farmers who grow chewing tobacco are gradually shifting to sugar cane, maize, potatoes, groundnut and mustard.

## INTRODUCTION OF LESS HARMFUL TOBACCO

In order to reduce the risk associated with smoking, attempts are being made all over the world to produce less harmful tobacco. It is well known that tobacco smoking is responsible for cancer, cardiovascular diseases and chronic obstructive lung diseases. The main constituents of smoke that are harmful to health are polycyclic aromatic hydrocarbons, carbon monoxide, hydrogen cyanide and *N*-nitrosamines. Having recognized the harmful

nature of tobacco smoke, the international cigarette industry developed three technologies to reduce these smoke constituents substantially, to offer a less harmful smoking product. These are: (i) modification of the blend; (ii) introduction of effective filters; and (iii) improving filter ventilation and paper porosity to dilute smoke. As a result, the average tar level of US cigarettes has been reduced to 15 mg/cig from 25 mg/cig. According to Wynder and Hoffmann (1) the maximal concentrations of tar and nicotine in the smoke of less harmful cigarettes should be 8 and 0.6 mg, respectively.

Ultra-low-tar cigarettes (5 mg tar and 0.1 mg nicotine) are now available on the international market. In India, filter cigarettes account for a little over 50% of total production (Table 4). The range of tar levels in Indian cigarettes is 20-30 mg/cig, and this needs further reduction. As filters and ventilation systems are expensive, blend modification offers a viable method under Indian conditions for preparing less harmful cigarettes. At the

**Table 4**  
*Production of cigarettes in India<sup>a</sup>*

Year	Quantity (million pieces)	Percentage (share of filter tips)
1981	86 938	30
1982	93 857	29
1983	80 445	42
1984	85 028	46
1985	80 680	56
1986 <sup>b</sup>	84 360	54
1987 <sup>b</sup>	75 420	51

<sup>a</sup>Source: Directorate General of Technical Development, Government of India

<sup>b</sup>Provisional, as published in *The Tobacco Reporter*

Central Tobacco Research Institute, a simple, inexpensive technology was developed to reduce the levels of harmful compounds, which involves application of potassium citrate to cigarette shreds so as to bring the potash level up



to around 3.5% (2). This modification resulted in a 35% reduction in total particulate matter and reduced the mutagenicity of smoke by 80%. The latter indicates a substantial reduction in the toxicity of cigarette smoke. It has been suggested that the Indian cigarette industry adopt a combination of the two technologies, i.e., filters on all brands and blend modification. Excise concessions for less hazardous smoking products will go a long way to ushering in the technologies for production of less hazardous smoking products in India.

### BY-PRODUCTS OF TOBACCO AND ITS WASTES

Acute awareness of the health hazards associated with smoking has resulted in a worldwide crisis for the tobacco industry. However, as described above, this crop cannot be replaced immediately in India. It is therefore important that the utilization of tobacco for alternative purposes be investigated. Tobacco contains certain phytochemicals which can be isolated

and converted into valuable products. Nicotine, solanesol, malic acid, citric acid and proteins can be isolated from tobacco. The availability of some of these phytochemicals in different types of tobacco wastes is shown in Table 5. Furthermore, tobacco seed contains up to 35% oil.

Nicotine, which can be converted to nicotine sulfate, is used as an insecticide. Being of plant origin, it may not have some of the drawbacks of synthetic insecticides, such as the induction of insect resistance, pest flare-back, secondary pest resurgence and pesticide residues. Nicotine is also used in the pharmaceutical industry in the form of nicotinic acid, nicotinamide and nikethamide. Solanesol is used as an intermediate in the synthesis of a cardiac drug and of vitamin K analogues. Malic acid and citric acid are used in the food and pharmaceutical industries.

Tobacco leaf proteins may find use for human consumption. At present, tobacco-seed

**Table 5**  
*Solanesol, nicotine and organic acid contents in various tobacco waste materials*

Tobacco waste material	Solanesol (%)	Nicotine (%)	Organic acids	
			Malic acid (%)	Citric acid (%)
Flue-cured tobacco scrap	0.9	1.7-2.8	5.0-6.3	2.0-3.1
Low-grade flue-cured tobacco scrap	0.6	1.8		
<i>Natu</i> scrap	0.1-0.2	2.9-3.3	10.5-12	3.0-4.0
<i>Bidi</i> scrap	0.5	8.9	7.5-8.7	3.5-4.0
<i>Kumkumadri (Bidi)</i> scrap	0.5	9.5	10.0	3.3
Cigar filler scrap	0.1	2.0	3.8	5.0
<i>Lanka</i> scrap	0.2	4.0-7.6	5.0	5.0
Factory waste (Imperial Tobacco)	0.1	1.5	4.0	3.0
Factory waste (Godfrey Philips)	0.1	1.4	4.0	3.0
Burley scrap	0.3	1.8	0.0	5.0
Factory waste (Golden Tobacco)	0.3-0.4	1.6	5.0	4.0
FCV midrib	ND	—	12.5	0.0
<i>Bidi (Kumkumadri)</i> midrib	ND	—	10.0	1.0
<i>Natu</i> midrib	ND	—	7.5	1.9

ND, not detectable



**Table 6**  
*Exportation of two tobacco phytochemicals, 1982-87*

Year	Nicotine sulfate		Crude solanesol	
	Quantity (tonnes)	Value (Rs. $\times 10^6$ )	Quantity (tonnes)	Value (Rs. $\times 10^6$ )
1982	346	25.9	60	9.2
1983	NA	—	30	4.7
1984	245	18.3	40	7.1
1985	417	31.2	NA	—
1986	560	42.0	NA	—
1987	226	16.9	NA	—

NA, not available

—, not applicable

oil is used in the paint industry as a semi-drying oil and has excellent potential use as an edible oil after refining.

India exports both nicotine sulfate and crude solanesol in substantial quantities to countries like Japan, the UK, the USA, Switzerland, Canada and Germany. Exports of these two products in 1982-87 are shown in Table 6. The availability of citric and malic acid in the country at the moment is limited.

#### PROBLEMS IN DISCONTINUING TOBACCO CULTIVATION:

- (1) revenue losses of Rs.14 000-16 000 million (US\$ 812-1123 million) in excise and foreign exchange earnings;
- (2) unemployment for hundreds of thousands of trained rural men and women, posing a social problem for the Government;
- (3) unemployment for workers in cigarette factories, established with huge investments;
- (4) aggravation of pesticide residue problems, since alternative commercial and food crops require heavy use of pesticides;
- (5) decreased security for farmers, since no other crop is as drought-tolerant;

- (6) unemployment for hundreds of thousands of tribal people who collect *tendu* leaves from the forests for the *bidi* industry;
- (7) lack of motivation from the Government and social agencies to persuade traditional tobacco farmers to cultivate profitable substitute crops; and
- (8) altered socioeconomic conditions of tobacco farmers if the present hectareage of 400 000 occupied by tobacco is utilized for the production of non-tobacco crops.

#### PLANS FOR ALTERED TOBACCO PRODUCTION:

- (1) evolve economically viable, tobacco-based cropping systems;
- (2) examine the potential of tobacco as an oil-seed crop;
- (3) examine alternative uses of tobacco: development of viable, integrated technology for the manufacture of edible proteins from green leaves of tobacco and for extraction of solanesol, nicotine sulfate, malic and citric acids from tobacco and tobacco wastes; and
- (4) identification and development of varieties to suit changing quality specifications in respect of tar and nicotine contents, with emphasis on export-quality tobacco.

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# Smokeless tobacco in the USA: usage patterns, health effects, and extent of morbidity and mortality

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In recent times there has been a revival in the use of smokeless tobacco in the USA. Currently, it is popular among male adolescents, young adults and other subgroups. Its use often preludes tobacco smoking and alcohol drinking. Smokeless tobacco contains several carcinogens, of which tobacco-specific nitrosamines are the most significant. Tobacco is a risk factor for oral cancer; evidence also suggests an association with cancers in other locations. Smokeless tobacco use is also associated with leukoplakia and other oral soft-tissue lesions, as well as gingival recession. Examination of trends in oral cancer incidence and mortality can be useful in monitoring long-term consequences of changes in smokeless tobacco use. There is an intense awareness of the adverse health consequences of smokeless tobacco use in the USA, and the US Congress has passed the legislation banning the advertising of smokeless tobacco products on television and radio as well as making it mandatory to put warning labels on all advertisements of smokeless tobacco products.

## INTRODUCTION

In the past 20 years, a revival in the use of smokeless tobacco, which includes chewing tobacco and snuff, has occurred in the USA, concentrated especially in adolescents and young adults. Overall, only 6% of adult men use smokeless tobacco in the USA (1), and morbidity and mortality associated with these habits are relatively low compared to that for cigarette smoking. Nevertheless, smokeless tobacco use is an established risk factor for oral cancer, and it is being used by young people, who may face long-term consequences of the habit. This paper describes the health consequences of the use of smokeless tobacco, the patterns of use of smokeless tobacco in America, and how smokeless tobacco compares as a public health problem to smoking in the USA. Comparisons will be made to the

experience in India with the use of unsmoked tobacco. The emphasis will be on recently emerging issues and research findings.

## SMOKELESS TOBACCO AND ORAL CANCER

Of the consequences of the use of smokeless tobacco, oral and pharyngeal cancers, which in the USA are associated with a 50% five-year survival (2), are the most severe. Case reports (3) provided the earliest evidence of the link between the use of smokeless tobacco and oral cancer, portraying patients with a long history of use of snuff or chewing tobacco (20 years or more) and with a squamous-cell carcinoma near the site where the tobacco had usually been placed.

Epidemiological studies have also supported the hypothesis that smokeless tobacco



use is a risk factor for oral cancer. My work in this area came as a result of observations made at the National Cancer Institute that oral cancer mortality rates among white women were exceptionally high in the south-eastern part of the USA during the period 1950-69 (4). We conducted a hospital and death certificate-based case-control study in the State of North Carolina (5). Women who were diagnosed with oral or pharyngeal cancer in five hospitals were interviewed in their homes using a standard questionnaire; data on women who died of these cancers were also included. Controls from the same sources with other diagnoses were similarly interviewed. We found that, among non-smoking women, snuff use was four times more common in the oral cancer patients than among the controls.

Subsequently, my colleagues and I at the National Cancer Institute undertook a much larger case-control study of oral and pharyngeal cancer (6). In this population-based study, cases were identified from four population-based cancer registries in the USA that covered the Atlanta, Georgia Metropolitan area, the State of New Jersey, Los Angeles, California, and two counties near San Francisco, California. To obtain population controls, we used two sources: random-digit dialling for younger controls (under age 65) and Health Care Financing Administration records for older controls. Random-digit dialling is useful for obtaining a probability sample of younger populations in the USA because of their high rate of telephone ownership. The Health Care Financing Administration has fairly complete records of older persons in the USA since nearly all elderly persons are covered by the Medicare programme. Controls were frequency matched to cases on age group, race and sex. Interviews were conducted with cases and controls or the next-of-kin of deceased subjects.

Alcohol drinking and cigarette smoking were strongly and synergistically associated

with oral cancer in this study. Smokeless tobacco use was examined as well; the proportion of male cases and controls who reported smokeless tobacco use was similar (6% and 7%, respectively), while among women, 3% of cases and 1% of controls used these products. No male case used smokeless tobacco to the exclusion of cigarette smoking, so the effect of smokeless tobacco could not be examined among men. Among the few women who used smokeless tobacco but did not smoke, we observed a six-fold increased risk (odds ratio = 6.2, 95% confidence limits of 1.9 and 19.8).

These findings are quite consistent with those of other case-control studies of smokeless tobacco use and oral cancer (7-11). In the USA, case-control studies have been virtually the only study design employed to examine cancer risks associated with smokeless tobacco use; the relative infrequency of the habit and the low incidence of oral cancer have made cohort studies impracticable.

A causal role for smokeless tobacco in the etiology of cancer has considerable biological plausibility. A number of carcinogens have been isolated from smokeless tobaccos (12), including tobacco-specific nitrosamines, polonium-210, benzo[*a*]pyrene, formaldehyde, acetaldehyde and crotonaldehyde (see paper by Hoffmann *et al.*, on smokeless tobacco, this volume). Of these carcinogens, the tobacco-specific nitrosamines, especially *N*'-nitrosonornicotine and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone, are the most significant. They have been shown to produce cancers in laboratory animals, and they are present in very high amounts in smokeless tobaccos. Smokeless tobacco users are exposed to quantities sufficient to cause cancer in laboratory animals. Although much of the critical epidemiological evidence on the carcinogenic potential involves populations using dry snuff, the moist snuff common in the USA and European snuffs all have high nitrosamine levels (13).



A number of scientific panels have concluded that smokeless tobacco is a cause of oral cancers. Among these groups are the International Agency for Research on Cancer (3) a National Institutes of Health Consensus Conference Panel (14) and an Advisory Committee to the US Surgeon-General (15).

## SMOKELESS TOBACCO AND OTHER CANCERS

Although most of the research in this field has been focused on the link between smokeless tobacco and oral cancer, some evidence links the habit to other cancer sites as well.

Several epidemiological studies have addressed whether oesophageal cancer is related to smokeless tobacco use (11,16-18). In the four case-control studies, relative risks ranged from 0.9 to 3.9. In only one study (18) were findings among nonsmokers reported, and so confounding by smoking status is a possible explanation for the many of these findings.

Bladder cancer has been the subject of a number of reports (19-24), and here the evidence generally points to no association between cancer at this site and use of smokeless tobacco products. The Advisory Committee to the Surgeon-General, which examined evidence for cancer at other anatomical sites, concluded that data on the topic were sparse or inconclusive.

In the USA, it has been extremely difficult to evaluate epidemiologically the relationship between smokeless tobacco use and cancer, for three reasons: the low incidence of cancer, the low frequency of the use of smokeless tobacco, and especially the absence of good controls for confounding from cigarette smoking. In many of the earlier studies, controlling for smoking was simply not addressed. In some later studies, either the frequency of smokeless tobacco use was so low that further cross-tabulation by smoking status was impossible, or the extremely high correlation of smokeless

tobacco and smoking habits was such that smokeless tobacco users were virtually all smokers. These problems are likely to persist in future studies in the USA.

## TRENDS IN USE OF SMOKELESS TOBACCO

Smokeless tobaccos, which include chewing tobacco and snuff, were the most popular forms of tobacco used in the USA at one time. Use of smokeless tobaccos declined from 1900 to the 1970s (25), at which time a resurgence of use of these products occurred (15).

A recent study from the National Center for Health Statistics (1) found that 6% of adult males use smokeless tobacco (Fig. 1),

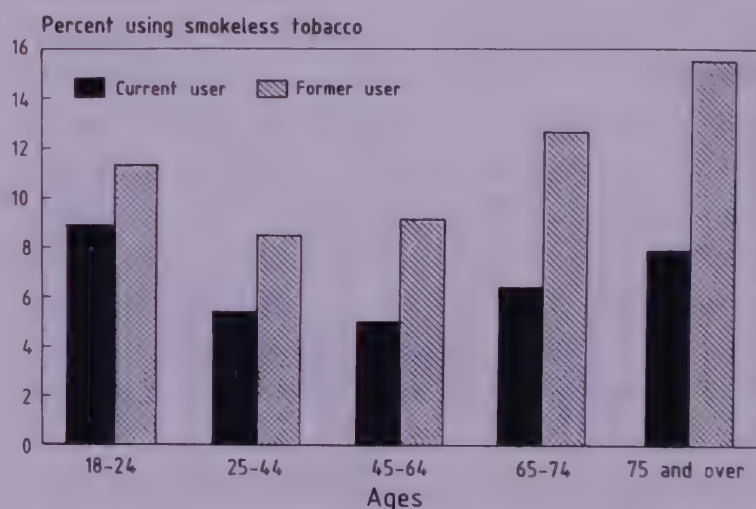


Fig. 1. Percentage of men using smokeless tobacco: USA (source: ref. 1)

translating into 4.9 million adult male users. Ten times as many men (49 million) smoke. Few American women, (0.6%), currently use smokeless tobacco products. These data are derived from the National Health Interview Survey and involve responses from more than 40 000 people who had household interviews and were part of a national probability sample. The findings are quite similar to those found in two other national surveys, conducted in 1986 (26,27). Use of smokeless tobacco among males is associated with a lower education and lower income (1,27).



White males are more likely to be users than black males (1,26,27). Some geographical variations in prevalence of use exist, as demonstrated by data from the Behavioral Risk Factor Surveillance System of the Centers for Disease Control (28). Areas where 6.5% or more of the men use smokeless tobacco include the south-eastern USA, extending to Illinois and West Virginia, and some north-western states.

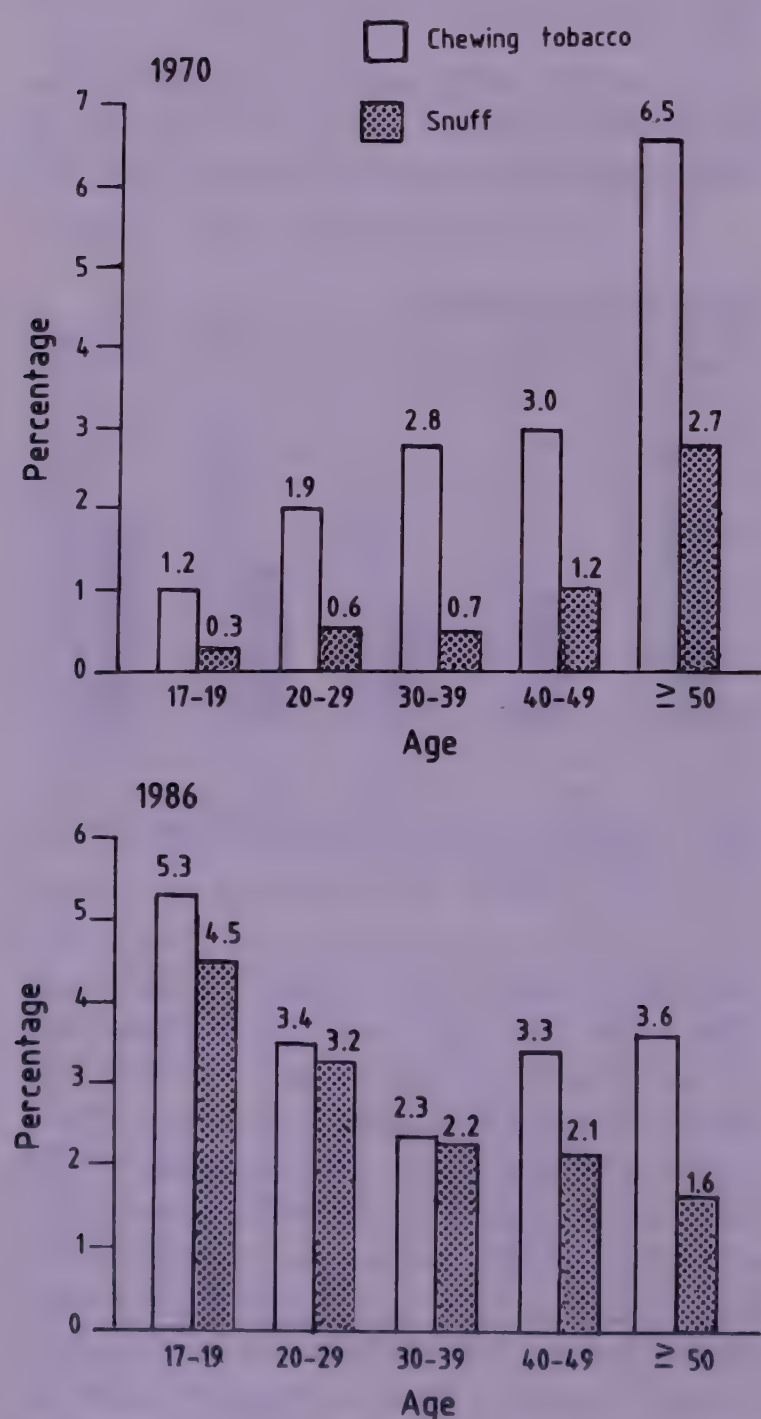


Fig. 2. Prevalence of chewing tobacco and snuff use among men, 1970 (NHIS) and 1986 (AUTS) (source: ref. 29)

In the USA, use of smokeless tobacco is concentrated in the elderly, who presumably acquired the habit in the earlier part of the century when the habit was common, and among youth influenced by recent trends. The trends in use of smokeless tobacco over the past two decades are illustrated by this comparison of age trends in smokeless tobacco between 1970 and 1986 (Fig. 2) (29). In 1970, the age group most likely to use smokeless tobacco was persons 50 years of age and older, in 1986, persons 17-19 years of age were the most likely to use these products.

Over the past 10-15 years, studies of smokeless tobacco use in regions of the USA have documented the prevalence of use among youth, and these have been summarized in a report by Boyd *et al.* (30) and in Tables 1 and 2. Studies of prevalence often were initiated because of a suspicion that the rates would be high. Among boys roughly aged 9 to 11, current use, often defined as use in the previous seven days, ranged from 2.8-11.9% in the studies described by Boyd *et al.* (30). At older ages, up to almost one-quarter of boys reported current use. Some of the psychosocial

Table 1

US regional studies of current use<sup>a</sup> of smokeless tobacco by boys

Age (years)	Users (%)
9-11	2.8-11.9
15-17	1.6-23.7

<sup>a</sup>Use in previous seven days

Table 2

General characteristics of youth using smokeless tobacco

- Use by boys common; use by girls uncommon
- Percent of ever users among boys
 

Age 9-11	16-57%
Age 15-17	26-78%
- Use begins very young
- Determinants of use may include smoking/alcohol/social factors



factors which seem to be linked to the adoption of a smokeless tobacco habit are use by peers and parents, smoking and alcohol use (31).

Other special populations in the USA in which use is concentrated are athletes (32) and native Americans (Table 3). Strikingly high rates of smokeless tobacco use, ever or current, occur among native Americans (33-37): up to one-third of native American adolescent populations report current use of smokeless tobacco. Oral soft-tissue lesions are also common in these groups (37). Most remarkable is the extensive use of smokeless tobacco among girls observed in these studies, 13-82% of whom had tried these products. In India, women who used *mishri* (burnt and roasted tobacco powder) were more likely to have low birthweight babies and a lower male to female sex ratio (see paper by Krishnamurthy, this volume). This fact raises concerns about potential reproductive effects of smokeless tobacco use in the USA among native American girls and suggests that research on this issue is needed.

**Table 3**

*Smokeless tobacco use in native American youth*

- 
- Very high prevalence of ever use: 27-88% of boys, 13-82% of girls
  - Very high prevalence of current use: one-third of boys and girls in some studies
  - In one study more than one-third of regular users had an oral lesion
- 

One major concern among health professionals is the extent to which smokeless tobacco serves as a 'gateway' to the initiation of other unhealthy habits. Historically, smokeless tobacco use has started at very young ages. In our study in North Carolina of older women with oral cancer (5), one-third had developed their habit by the age of 10. Studies of today's youth also suggest that use begins at an early age (38). The concern is that these smokeless

tobacco-using youth will switch to cigarettes later. A few studies provide data on this question. In one, initiation of use of smokeless tobacco and smoking was investigated among boys aged around 15 years in Washington State (39). The boys completed a questionnaire on habits, which included data on the ages at which various habits were started. The results revealed that smokeless tobacco use is a risk factor for initiation of smoking and also for using the product at least weekly. The converse was also true. Cigarette smokers were more likely than nonsmokers to take up a smokeless tobacco habit and to use smokeless tobacco weekly.

One longitudinal study followed 1676 boys in Oregon for one year (40). Boys who were using smokeless tobacco at base-line were found to be much more likely to acquire a cigarette habit or to drink alcohol within one year. Whereas 5.8% of smokeless tobacco users developed a smoking habit, only one-half of a percent of nonusers of tobacco developed the habit. Among those boys who already smoked cigarettes or used alcohol, those with a smokeless tobacco habit were more likely to increase their consumption of cigarette smoking or alcohol drinking. The investigators noted similar findings in a separate longitudinal study of adolescents (41).

While educational programmes have been devised to prevent initiation of smokeless tobacco in young people, little evaluative research has been done to determine what works. Likewise, the data available on cessation programmes are limited. One investigator who was experienced in conducting smoking cessation clinics adapted the programme for smokeless tobacco users (42). His success rate at six months was only 2%, although his average for smokers was 38%. This finding contrasts with the success of large-scale intervention studies in India addressing smokeless tobacco and smoking cessation among adult populations (43).



## TRENDS IN ORAL CANCER INCIDENCE AND DEATH RATES

Over the past 40 years, incidence rates among white men for oral and pharyngeal cancer have been steady, while rates among white women have increased by 50%. The steady rates over time among men are the result of declining rates in older men, presumably because of declines in the use of smokeless tobacco, pipes and cigars, and of increasing rates in younger men, probably due to smoking. The increases in oral cancer rates among women parallel the adoption of cigarette smoking (44). Trends in oral cancer incidence and mortality are especially interesting in two special subgroups of the population: women in south-eastern USA and young adults.

High mortality rates from oral cancer among white women in south-eastern USA (depicted on colour maps of mortality for the period 1950-69) provided the impetus for my research on this topic. Subsequently, the National Cancer Institute produced a new set of maps depicting cancer mortality, this time for 1950-80, separately for each decade (45). The map for 1950-59 shows the 'epidemic' of oral cancer in the south-east; however, by 1970-80 this epidemic had 'dissolved'. In south-eastern USA, oral cancer mortality rates among white women are decreasing at a rate significantly greater than the trend for all of the USA. In contrast, major metropolitan areas, such as Los Angeles, New York and Chicago, are experiencing upward trends in oral cancer rates relative to the total US experience. Presumably, this rise is due to increasing smoking rates in these urban areas and reduced use of smokeless tobacco in the south-east.

Thus, this particular epidemic seems to be resolving. However, there remains cause for concern about a potential epidemic of oral cancer among young adults in the USA as a result of heavy use of smokeless tobacco at young ages. The evidence to date is not strongly

supportive of an emerging epidemic of oral cancer in youth as a result of the increasing use of smokeless tobacco; however, there are a few unsettling observations. One is a celebrated case of tongue cancer in a youth who had a long-standing snuff habit (46). The mother of the youth brought a legal suit against the company which produced the tobacco (but lost). There are anecdotal reports of other males in their late teens or early adulthood who have developed oral cancer as a result of smokeless tobacco use. There are also a few investigations of an increase in the incidence of tongue cancer in young adults, hypothesized to be due to trends in the use of smokeless tobacco (Table 4).

**Table 4**  
*Oral cancer in young adults*

Study	Ref. no.	Increases over time
Univ. of Texas 1944-84	47	In number and % of all cancers
9 SEER areas 1973-84 (Incidence)	48	By 1.8 fold among 30-39-year olds, by 1.3 among 10-29-year olds
US mortality 1950-82	49	Among 10-29, 30-34, and 35-39-year olds

The University of Texas study involved an examination of trends in hospital admissions for cancer; increases were observed over the 40-year period in the number of tongue cancer cases and in tongue cancer as a proportion of all cancers (47). Rates were computed in the other three studies. Both of the US studies, one of incidence (48), the other of mortality (49), suggest an increase in the rates of tongue cancer; in the mortality study, rates of other oral cavity cancers were not rising. While these increases were hypothesized to be due to smokeless tobacco usage trends, it is not possible to be certain of the determinants without more careful study.



It has proven difficult to examine oral cancer trends in youth. A low base-line incidence rate is the primary reason; even among men aged 35-39, oral cancer occurs with a frequency of only 3.5 per 100 000 men per year (50). Smokeless tobacco-using cancer patients may wish to bring legal action against a tobacco manufacturer, making epidemiological investigations difficult. Finally, assessing which of the potential risk factors might be responsible for a change in incidence of a rare and multifactorial cancer site is very difficult.

### HEALTH CONSEQUENCES — SMOKELESS TOBACCO *VERSUS* SMOKING

Cigarette smoking is a cause of a wide array of serious medical conditions, including coronary heart disease, atherosclerotic peripheral vascular disease, chronic obstructive pulmonary disease, cancers of the lung, larynx, oesophagus, oral cavity and pharynx, and low birthweight babies (see papers by Paffenbarger *et al.*; Sasco; and Gortmaker *et al.*, this volume). An estimated 390 000 deaths in the USA annually are attributable to smoking (29). In contrast, oral cancer is the only cancer conclusively linked to smokeless tobacco use, and cancer is the only life-threatening condition associated with use of these products. Oral cancers account for 2% of all cancer deaths among US men and 1% among women (2). This finding is in marked contrast to the large proportion of deaths in India attributable to oral cancers.

Attributable risk is defined as the proportion of disease in the population which

could be prevented if the risk factor could be removed. In the most recent Surgeon-General's Report, an estimated 92% of oral cancers among men and 61% of oral cancers among women could be prevented if smoking could be eliminated (29). In India, the tobacco associated attributable risk ranged from 70% to 84% for oropharyngeal cancers (see paper by Jayant and Yeole, this volume). Because a large proportion of oral cancer among men in the USA is due to cigarette smoking, the contribution of smokeless tobacco to overall oral cancer mortality is small. Among American women, the prevalence of smokeless tobacco use is extremely low, and so the impact of smokeless tobacco on the overall oral cancer disease burden is exceedingly small. Nevertheless, the impact of smokeless tobacco has been significant in some settings. We estimated that 87% of gingival and buccal mucosal cancers among women in south-eastern USA were attributable to the use of snuff and that snuff use accounted for the high rate of oral cancer there (5).

### SMOKELESS TOBACCO AND ORAL SOFT-TISSUE LESIONS

While an epidemic of mouth cancer arising from use of smokeless tobacco has not been demonstrated conclusively, there are other documented consequences of the use of smokeless tobacco in youth. Oral soft-tissue lesions are frequently observed in users of smokeless tobacco (Table 5). Three studies (51-53) have specifically addressed the occurrence of oral lesions in US grammar school (roughly, ages

**Table 5**

*Prevalence of oral soft-tissue lesions in smokeless tobacco-using youth and adults*

Population	Ref. no.	Prevalence (%)	Type of lesion
Rural students in Colorado	52	63	Modified Axell scale
Urban students in Colorado	51	49	Modified Axell scale
Students in Georgia	53	23	Furrowing, white, opalescent
Finnish military recruits	54	44	Wrinkled, gray/white, elevated



10-13) and high-school youth. Use of smokeless tobacco in these studies of 400-1100 students ranged from 11-13%. Oral lesions, detected by trained oral examiners unaware of the students' tobacco habits, were found in 23-63% of those reporting current use of smokeless tobacco; the prevalence of lesions in nonusers of smokeless tobacco was apparently 0%.

In two of the studies, the appearance of the lesions was classified according to a scheme developed by Greer and Poulson (51) into three degrees: from mild lesions, involving slight wrinkling and no colour changes, to degree-three lesions with furrows, thickening/wrinkling of the mucosa and colouring of red or white. While 41-50% of the lesions were degree-one or mild, 14% of the lesions in one study (51) and one-third of the lesions in the other (52) were classified as degree-three. Lesions were localized in those areas of the anterior oral vestibule where the tobacco was routinely placed. In the third report, the lesions were described as involving 'a mild increase in opalescence and whiteness, with slight furrowing' (53). A study of Finnish military recruits (54) found that 11% of the 441 recruits used oral snuff, and 44% of those users had lesions described as 'grayish white, wrinkled and elevated'. In a recent study of adolescent athletes, leukoplakia was found in 5% among the 8% of the athletes using smokeless tobacco (55).

Biopsies were not usually done in these studies of high-school students. However, in the Finnish study, biopsies of the lesions showed a variety of abnormalities, including epithelial thickening and partial keratinization (54).

In the USA, professional baseball players have a long-standing reputation for using smokeless tobacco. A recent study of these players (56) has shown a high prevalence (36%) of use of these tobacco products and a high (27%) frequency of oral lesions among

users. The investigators estimated that users were five times more likely to have a soft-tissue lesion than controls.

Leukoplakia is well known to be present concurrently with oral cancer in older people (3); also, areas of leukoplakia, especially nodular leukoplakia, undergo malignant transformation (57). Less is known about the natural history of these less severe lesions, which appear with such high frequency in young users or long-term users. Of the two Colorado studies, one reported that two of the students were aware that a white oral 'callous' had disappeared after they stopped their smokeless tobacco habits (51). There also seems to be considerable anecdotal evidence from dentists who see these lesions and state that they disappear with discontinuation of use of the product or movement of the tobacco to another place in the mouth. The Finnish study also found that the few recruits who had stopped their snuff habit had a normal oral mucosa, suggesting that any changes that had been evident before had regressed (57). The characteristics of oral soft-tissue lesions in youth are summarized in Table 6.

**Table 6**  
*Oral lesions in smokeless tobacco-using youth*

- 
- Very common
  - Many are degree-1
  - Not associated with pain/discomfort
  - Often reported seeing a dentist recently
  - Occur in heavy users of smokeless tobacco
  - Can appear with short duration of habit
  - Regression with disuse of smokeless tobacco
- 

Besides the oral mucosal lesions found in smokeless tobacco users, the other major oral consequence of smokeless tobacco use is gingival recession (58). Numerous case reports describe gingival recession in smokeless tobacco users. Several cross-sectional studies, involving dental examinations and questionnaire administration, have also provided



information on this consequence of smokeless tobacco use (Table 7). Gingival recession was evident on at least one surface in 26-60% among the smokeless tobacco-using adolescents and young adults in these studies. The applicability of these findings to Indian populations using tobacco-containing *pan* (betel quid) is unclear. In the USA, gingival recession would appear to be directly associated with the physical placement of smokeless tobacco, especially snuff, in specific areas adjacent to the teeth and gingivae for prolonged periods.

**Table 7**

*Gingival recession in smokeless tobacco-using adolescents<sup>a</sup>*

Population	Ref. no.	Sample	% with gingival lesions
Urban students in Colorado	51	117	26
Rural students in Colorado	52	56	27
Students in Georgia	53	75	60

<sup>a</sup>Adapted from: ref. (58)

## SMOKELESS TOBACCO USE AND OTHER HEALTH EFFECTS

Smokeless tobacco contains nicotine. The maximum levels of nicotine in smokers and snuff users are similar. Among smokeless tobacco users, peak levels are achieved as rapidly as for smokers, but these levels remain higher for a longer period of time than among smokers (59).

Some of the reported health effects derive from the nicotine content of the smokeless tobaccos. Increased blood pressure and heart rate have been observed in people studied under laboratory conditions during and after use of smokeless tobacco and smoking products (59). Nicotine may not be the only contributor to blood pressure effects, as sodium levels are high in some brands (60). Smokeless

tobacco use has been linked to hypercholesterolaemia in one epidemiological study (61). In that study, 2840 men, who were part of a health examination programme, received a questionnaire on habits, underwent a fitness test and had blood drawn. The 93 smokeless tobacco users were found to be 2.5 times more likely than nonusers to have hypercholesterolaemia, defined as a serum cholesterol level of 6.2 mmol/L or greater, than nonusers, controlling for age, education, fitness and smoking. Relative risks were smaller for daily smokers of 1-20 cigarettes and more than 20 per day, who had 1.5 and 2.0 times the rate of hypercholesterolaemia, controlling for smokeless tobacco and other factors.

## SMOKELESS TOBACCO PRODUCT LABELLING

Partly out of concern for the rise in use of smokeless tobacco by young men and boys, the US Congress passed legislation in 1986 which banned radio and television advertising for chewing tobacco and snuff and which required warning labels (Table 8) for all smokeless tobacco products and advertisements.

**Table 8**

*Warning labels for smokeless tobacco products and advertisements*

- Warning: This product may cause mouth cancer
- Warning: This product may cause gum disease and tooth loss
- Warning: This product is not a safe alternative to cigarettes

## CONCLUSIONS

Epidemiological research has conclusively linked smokeless tobacco use to the risk of mouth cancer. Evidence suggests associations with cancers at other sites; however, definitive epidemiological research concerning these sites is lacking because of the difficulty involved in studying a relatively rare 'exposure' and a rare cancer. Work on carcinogenesis and the role of tobacco-specific nitrosamines supports the epidemiological findings.



There appear to be decreasing oral cancer rates in very elderly populations in which use of smokeless tobaccos is declining, but some evidence suggests an increase in oral cancer incidence and mortality rates in younger adults. However, the role of smokeless tobacco in contributing to these increases is unclear.

A number of special subgroups of the US population use smokeless tobacco extensively and should be the focus of further epidemiological studies. These heavy users include male adolescents and young adults, native Americans and residents of certain US geographical areas.

The sustained epidemic of smokeless tobacco use has led to examination of health effects other than cancer. Most significant are the oral lesions arising in smokeless tobacco users. A fuller understanding of the natural history of these lesions is needed. The follow-up and re-examination of people with lesions

will be critical to monitoring the progress of these lesions. We need to understand better the pathological processes involved. In particular, it will be important to learn more about the role of viruses, in view of work on human papillomaviruses in the etiology of oral cancer and the potential for interaction of viruses and tobacco and other co-variables (62). These studies should involve populations among whom use of smokeless tobacco is exceptionally common. Studies involving questionnaires and dental and biochemical assessments will be especially useful in furthering our knowledge. The ongoing studies of California baseball players include many of these critical features (56).

A recent study reported that smokeless tobacco users are more likely to have hypercholesterolaemia (61). This is intriguing and should be followed-up with additional analytical epidemiological studies.

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# **CONSEQUENCES FOR ORAL HEALTH**





# An overview of research on oral cancer and precancer at the Basic Dental Research Unit

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Since 1966 the Basic Dental Research Unit has undertaken extensive epidemiological studies on oral cancer and precancer in seven areas of India and among Bombay policemen. Using a house-to-house approach, the tobacco habits of well over 200 000 villagers were recorded by trained interviewers. Cross-sectional studies were then carried out in which these individuals were examined by dentists for the presence of oral cancer and precancerous lesions, and about 66 000 of the villagers in four cohorts were re-examined annually over 10 years. All oral lesions were photographed in colour, and several hundred biopsies and smears for cytological examination were obtained from the lesions. Oral cancer and precancerous lesions were strongly associated with tobacco use, and in most instances the oral cancer originated from precancer. It was also demonstrated that it is possible to make people quit their tobacco habits, thereby leading to a decreased incidence of precancer. Several other strategies for the control of oral cancer were tried, such as using basic health workers for primary and secondary prevention and mouth self-examination techniques for early detection; these are being further investigated.

## INTRODUCTION

As early as 1908, a high frequency of oral cancer was observed in some parts of India (1,2) and was suspected to be due to the widespread habit of betel-quid chewing — a habit unknown in the western world. Subsequently, several studies convincingly demonstrated the aetiological role of betel-quid chewing and other forms of tobacco use in oral cancer (3-7).

Oral cancer was often observed to be preceded by or associated with leukoplakia, i.e., a white patch in the oral mucosa. This lesion was thus termed precancerous. The distribution of the location of leukoplakias and their association with tobacco habits were similar to those seen in cases of oral cancer. Furthermore, leukoplakias generally occurred in individuals who were younger than oral cancer patients. Studies among 4000 Bombay policemen (8) and surveys among 35 000

dental out-patients in four cities in India (9-12) showed that the prevalence of leukoplakia was high and that it was strongly associated with tobacco chewing and smoking. Very little information was available, however, from population-based studies on the prevalence and incidence rates of oral cancer and precancer and the natural history of oral precancer.

In 1964, the Basic Dental Research Unit was established at the Tata Institute of Fundamental Research with the objective of investigating the natural history of oral precancer, with the ultimate aim of developing preventive strategies for oral cancer. The hypothesis was that better knowledge of oral precancer would help in evolving effective strategies for primary and secondary prevention of oral cancer. A grant was obtained from the National Institutes of Health, USA. Following this, in 1966, extensive



epidemiological studies were initiated among 50 915 villagers in five districts of four states of India.

## MATERIAL AND METHODS

On the basis of results from prior studies (9-12), several methodological points were considered for our investigation. It was decided to concentrate on population-based epidemiological studies. The above studies conducted on specific occupational groups or hospital out-patients presented problems for generalization; our studies were therefore designed to be population-based. To make samples truly representative of the population, it was decided that the individuals would be examined on a house-to-house basis rather than inviting them to a central place for interview and examination. It was also planned to undertake the investigation in rural areas, as very little was known about the type or extent of tobacco use and oral cancer problems in rural India, where over 85% of the population lives. Accordingly, a methodology conducive to rural rather than urban areas was developed. As per the study design oral examinations were conducted by dentists, adopting internationally accepted, standardized diagnostic criteria.

The research started as an Indo-US Collaborative Project with Professor Jens J. Pindborg of the Royal Dental College and Dental Department, Rigshospitalet, Copenhagen, Denmark, as the co-principal investigator and Dr James E. Hamner, who is currently at the University of Tennessee, as the National Institutes of Health (NIH) Project Officer. This research is continuing in a phased manner under the same arrangement. The research conducted over the past 24 years can be divided into four phases; phase 1 (1966-69) consisted of cross-sectional surveys; phase 2 (1969-77) comprised follow-up studies of cohorts of individuals; and phase 3 (1977-88) was the behavioural intervention study for primary

prevention of oral cancer. In the ongoing phase 4 of the investigation, the emphasis is on evolving additional strategies for oral cancer prevention. The division into four phases is conceptual rather than chronological, as various phases overlap.

**Phase 1:** Cross-sectional studies, which began in 1966, were conducted in seven areas of India (Fig. 1). The sample size in these surveys ranged from 5000 to over 100 000, totalling about 200 000 individuals. In Ernakulam, Srikakulam, Bhavnagar, Darbhanga, Singhbhum and Goa, villages were sampled randomly. The most important findings to emerge from these studies were that tobacco use was very common and was practised as various different forms of chewing and smoking (see paper by Bhonsle *et al.*, this volume). The studies also characterized the prevalence rates of oral cancer and precancerous lesions and conditions, their association with different tobacco habits, and the clinical, cytological and the histological features of these lesions (13).

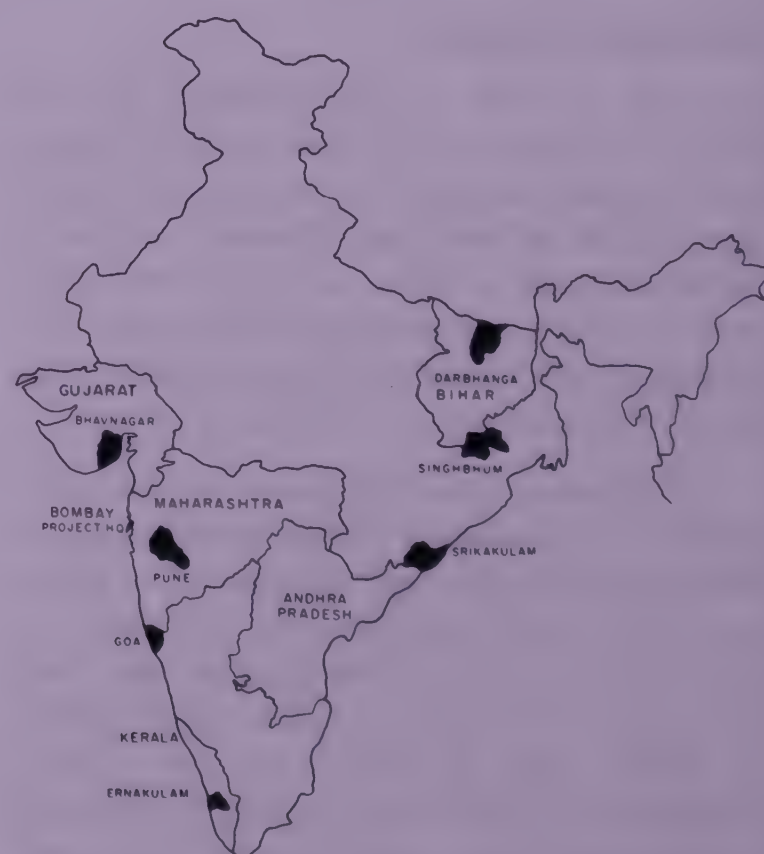


Fig. 1. Map of India showing areas of investigation



**Phase 2:** This phase consisted of follow-up studies of four cohorts, each for 10 years. The original cohort of 4000 Bombay policemen (8) was followed-up after interval of 5 and 10 years (14, 15); and three cohorts of over 10 000 individuals each were followed up annually in Bhavnagar, Ernakulam and Srikakulam. Major findings from this phase were that all new leukoplakias developed only among tobacco users, and that oral cancer was almost always preceded by a clinically diagnosable precancerous state (16). This phase also provided the malignant transformation rates for different lesions, their natural history (such as persistence, regression and recurrence) and the long-term behaviour of epithelial dysplasia.

**Phase 3:** Phase 3 consisted of the intervention study. Its main objectives were to educate tobacco users to stop their tobacco habits and to study the effect of habit cessation on the risk for oral precancer. For this study three cohorts, each of 12 000 tobacco users, in Bhavnagar, Ernakulam and Srikakulam districts were selected. The results after one, five and eight years (17-19) of intervention showed that it was possible to educate and motivate villagers to stop their tobacco habits and that this led to a reduction in the risk for oral cancer. The 10-year results showed similar results (see paper by Gupta *et al.*, this volume).

**Phase 4:** The results from phases 1, 2 and 3 demonstrated that primary and secondary prevention of oral cancer was feasible, at least in the research that had been set up. Phase 4 was initiated with a view to finding out whether primary and secondary prevention of oral cancer was feasible within the existing health care infrastructure. In the first study, some 53 basic health workers of the Kerala Government Health Department in Ernakulam district, were trained to identify high-risk individuals and precancerous lesions and in early detection of oral cancer. During their routine house-to-house visits, the health workers examined about 39 000 high-risk individuals;

they detected 20 oral cancers during one year. Estimates of the specificity, sensitivity and predictive values of their diagnoses were found to be within acceptable limits (20).

It has been our experience that even after early detection of oral cancer, individuals do not opt for treatment and do not therefore get the benefit of early detection (21). In order to motivate such individuals, as well as testing a new, low-cost strategy, the concept of mouth self-examination is being tried for early detection of oral cancer. Individuals in selected villages are being educated and motivated to conduct mouth self-examination and are being monitored for the efficacy of early detection of oral cancer through this method. The acceptability, feasibility and compliance rates are also being investigated.

Another strategy being tested in this phase is the use of basic health worker level individuals, in the prevention of oral cancer. In Srikakulam district, five such workers were trained in primary prevention and early detection of oral cancer, and each was assigned a group of villages in which they screened the population for oral cancer and precancerous lesions and implemented health education programmes on tobacco. They referred individuals with precancerous lesions to the temporary clinics set up and run by our research team for evaluation and other diagnostic procedures.

## DISCUSSION

This project is probably the longest running Indo-US collaborative research in the health field. The research outlined above led to many important new findings and confirmed several conjectures and hypotheses. The methodology adopted has been expensive, time-consuming and laborious, but it has paid rich dividends. It has led to findings that would not otherwise have been possible: e.g., tobacco use in various forms was found to be highly prevalent in rural population; oral precancerous lesions developed preponderantly among tobacco users;



oral cancer developed mostly among individuals with oral precancer; and it was possible to educate villagers about their tobacco habits and such education led to a decrease in the risk of oral cancer. These findings and several other research papers have been published and presented at numerous national and international conferences. The findings have made a significant impact in India as well as abroad, because of their great practical relevance. As a mark of recognition, the Basic Dental Research Unit was designated as the WHO

Collaborative Centre for Oral Cancer Prevention in 1986, so that it could offer its expertise and technical and academic collaboration as well as guidance for other researchers in this field.

### Acknowledgments

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# Reverse *chutta* smoking and palatal lesions

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In Srikakulam district, Andhra Pradesh, India, *chutta* is often smoked with the lighted end inside the mouth. This habit is responsible for the high incidence of palatal cancer and for specific palatal changes. Palatal changes are precancerous, and they include several components, such as keratosis, excrescences, patches, red areas, ulcerations and non-pigmented areas. Red areas appear to be the most dangerous and histologically: 52% of them exhibit epithelial dysplasia. Over a 10-year period, 10 palatal cancers arose, all from pre-existing palatal changes; malignant transformation occurred only in red areas and patches. During the same period, 75% of the palatal changes remained stationary and 14% regressed spontaneously. Cessation of the habit led to higher regression rates of palatal changes, and currently this appears to be the most effective method for managing palatal changes.

## INTRODUCTION

*Chutta* is a kind of cigar which is often smoked in reverse (i.e., with the lighted end inside the mouth) in certain coastal districts of Andhra Pradesh and adjoining regions of India (see paper by Bhonsle *et al.*, this volume). The palatal mucosa is thus exposed to pyrolysed tobacco products and intense heat: the temperature of the mucosa was recorded as 58°C during reverse *chutta* smoking (1). Although reverse smoking has been reported in several regions in the world (see paper by Pindborg *et al.*, this volume), few studies have been reported of its effect on oral health. In this paper, we describe the effects of this form of smoking on the palatal mucosa on the basis of extensive epidemiological studies conducted in Srikakulam district over the past 24 years.

## EFFECTS OF REVERSE SMOKING ON THE PALATAL MUCOSA

The most serious outcome of reverse *chutta* smoking is oral cancer, specifically squamous-cell carcinoma of the palate, and precancerous palatal changes.

**Palatal cancer:** Palatal cancer is uncommon in areas where reverse smoking is not prevalent. For instance, palatal cancer constituted only 3-12% of oral cancers in hospital-based studies in areas where reverse smoking is not practised (2-5). In contrast, in Visakhapatnam district, which borders Srikakulam district and where reverse smoking is also widespread, palatal cancers formed up to 48% of oral cancers among hospital admissions (6,7).

**Epidemiology:** In a cross-sectional epidemiological study of 10 169 villagers, 10 oral cancers (98 per 100 000) were diagnosed; nine of them were palatal cancers and all occurred among reverse smokers (191 per 100 000) (8). In a 10-year follow-up study of these individuals, the annual age-adjusted incidence rate of oral cancer was 37 per 100 000 among reverse *chutta* smokers; 10 of the 11 cancers were palatal cancers (9).

**Clinical aspects:** Palatal cancer occurred more often among women, and reverse smoking was more widespread among them. An early palatal cancer may appear like a thick



keratotic patch (Fig. 1) or as a small, deep ulceration. Generally, individuals with this disease do not seek medical attention until the lesion is advanced. With time, the lesion may assume a large exophytic mass filling the entire palate, or the ulcerative lesion may advance and perforate the palate (Fig. 2). Palatal changes may often be discerned adjacent to the cancer.

**Palatal changes:** Conventional pipe, cigar, cigarette or *bidi* smoking produces leukokeratosis nicotina palati, also known as smokers'

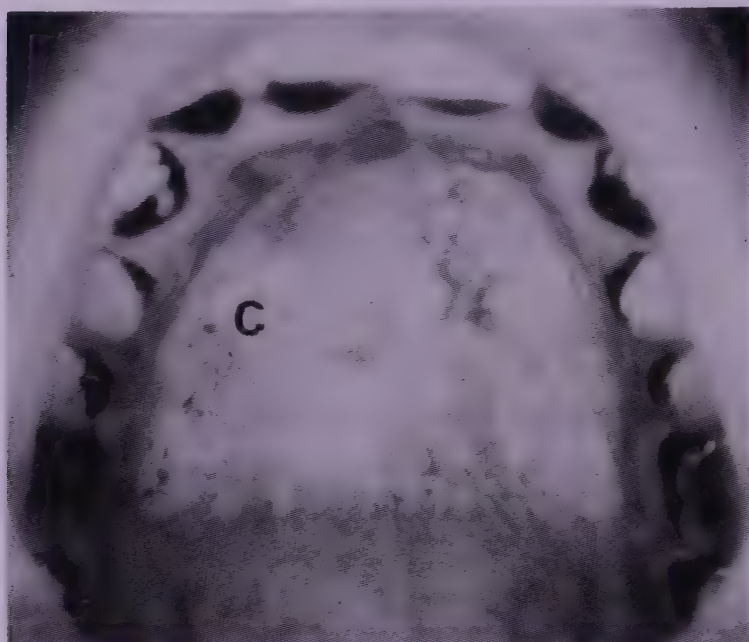


Fig. 1. Palatal cancer (C) appearing as a thick patch

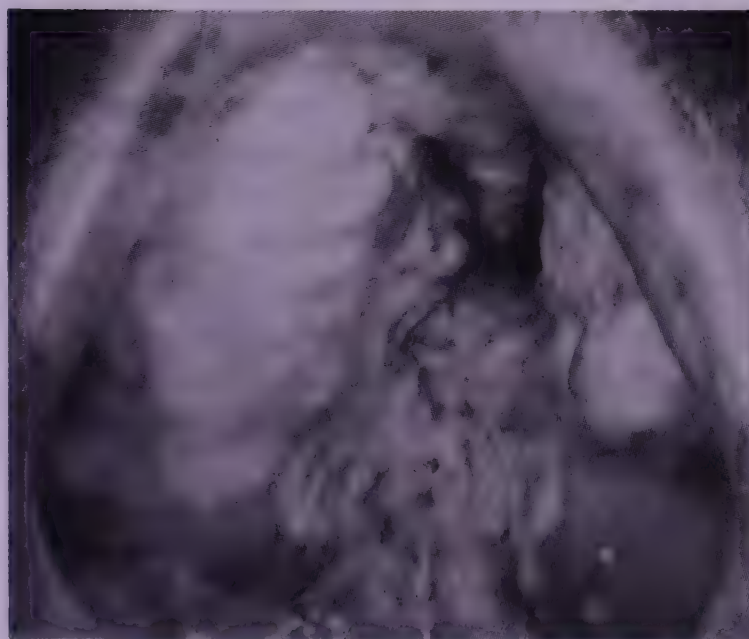


Fig. 2. Ulcerative cancer with palatal perforation

palate. This is characterized by whitening of the palatal mucosa, with small umbilicated excrescences corresponding to the orifices of the palatal salivary glands. These lesions are reversible if smoking is discontinued. Epithelial dysplasia is rarely found, and these lesions are not considered precancerous (see paper by Murti *et al.*, this volume). In contrast, reverse *chutta* smoking produces a spectrum of diverse palatal changes (9,10), which are precancerous (9). In the first study in Srikakulam district (8), the prevalence of palatal lesions among reverse smokers were recorded as 8.8% leukoplakia, 4.6% preleukoplakia and 17.9% leukokeratosis nicotina palati. Palatal involvement was noted in 422 (85%) of the 497 leukoplakia cases and in 168 (57%) of the 296 preleukoplakias, and of course in all of the cases of leukokeratosis nicotina palati. Palatal changes associated with reverse smoking thus exhibited spectrum of clinical changes, and it was not satisfactory to group them under leukoplakia, preleukoplakia or leukokeratosis nicotina palati. Accordingly, a new classification for palatal changes encompassing the entire spectrum of clinical components was proposed (9,10). The annual age-adjusted incidence rates of palatal changes (encompassing all components) was 24.9 per 1000 among men and 39.6 per 1000 among women, and the peak incidence was in the 55-64 year age group (9).

**Clinical aspects:** Palatal changes comprise several components (Fig. 3A and B): (i) *keratosis* — diffuse whitening of the entire palatal mucosa; (ii) *excrescences* — 1-3-mm elevated nodules, often with central red dots corresponding to the openings of the palatal mucous glands; (iii) *patches* — well-defined, elevated white plaques; (iv) *red areas* — well-defined reddening of the palatal mucosa; (v) *ulcerated areas* — crater-like areas covered by fibrin; and (vi) *non-pigmented areas* — areas of palatal mucosa that are devoid of pigmentation.

Various of these components occur independently (Fig. 3A), but more often they



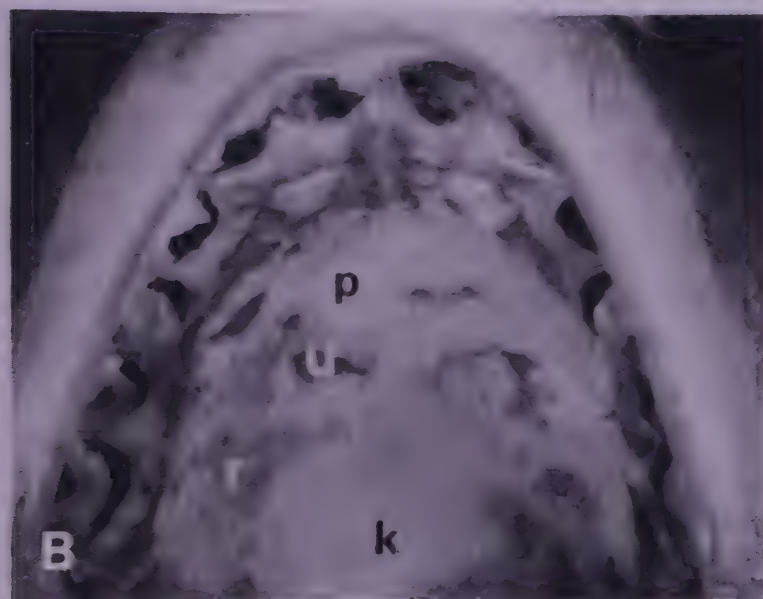
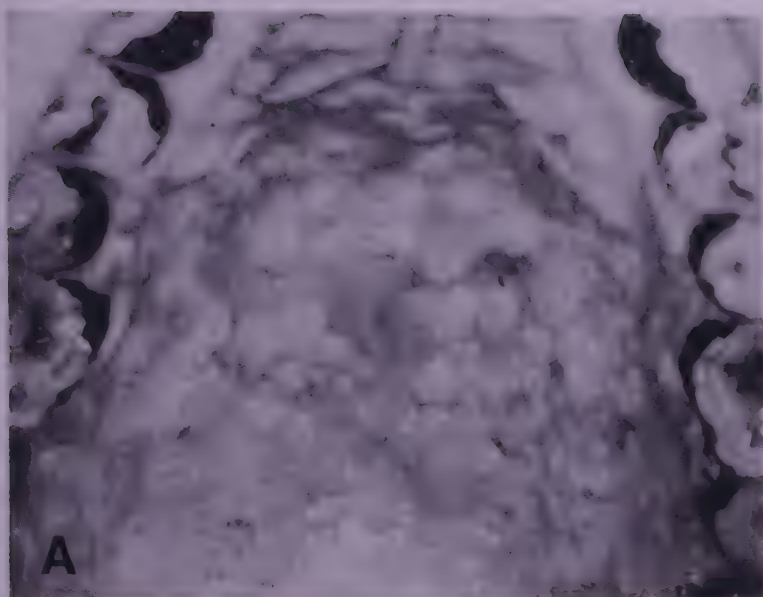


Fig. 3A. Excrescences characterized by 1-3 mm nodules

Fig. 3B. Co-existent palatal changes: (k) keratosis; (p) patch; (r) red area; (u) ulcerated area

co-exist (Fig. 3B). Although the definitions of patches, red areas and excrescences appear to be analogous to those of leukoplakia, erythroplakia and leukokeratosis nicotina palati, the special nomenclature was suggested in view of the very frequent co-existence of various components of palatal changes and their interchangeability over time.

**Co-existence:** Palatal changes can co-exist with non-palatal lesions. In a sample of 2710 reverse smokers with precancerous changes, palatal changes alone were observed among 94.6% of individuals, non-palatal lesions alone among 0.2% and a combination of palatal and

non-palatal lesions among 5.2% (9). The components of palatal changes can also co-exist (Table 1). Keratosis and excrescences co-existed most frequently; the combination of excrescences and patches was also common. Almost the same number of red areas occurred either singly or with patches or excrescences. All three components were present in 19 individuals. Palatal keratosis was observed exclusively among 569 individuals.

**Table 1**

*Co-existence of the components of palatal changes in Srikakulam district<sup>a</sup>*

	Red areas	Patches	Excrescences
Red areas	23	25	22
Patches	25	175	194
Excrescences	22	194	1679

<sup>a</sup>Source: ref. (9)

Keratosis only - 569

Patches+red areas+excrescences - 19

The diagonal terms denote only one component

In several instances, there was interchangeability over time between patches and red areas and red areas and patches, and sometimes between excrescences and patches. These observations imply that various components of palatal changes are interrelated and belong to the same spectrum of clinical change rather than as independent entities.

**Histological features:** The histological characteristics of the various components of palatal changes were studied in 101 biopsies (10). Hyperorthokeratosis, epithelial dysplasia and inflammatory cells in the connective tissue were observed in 87%, 23% and 55% of the biopsies, respectively. Melanin deposits were noted in the lamina propria of most of them. The epithelium was atrophic in 60% of biopsies from red areas. Epithelial dysplasia was observed in 52% of red areas, 25% of excrescences, 20% of ulcerations, 10% of patches and in 19% of non-pigmented areas.



*Natural history:* In a six-year follow-up study, palatal changes remained stationary in 75% of individuals, regressed in 14% and were variable in 11%, i.e., they regressed, recurred and regressed again (9). The regression was spontaneous, but the regression rates were higher when the habit was discontinued or reduced substantially (10,11); 90% of the excrescences regressed when the habit was discontinued as compared to 37% when there was no discontinuation (10). Similarly, 78% of the patches regressed when the habit was given up, as compared to 37% spontaneous regression.

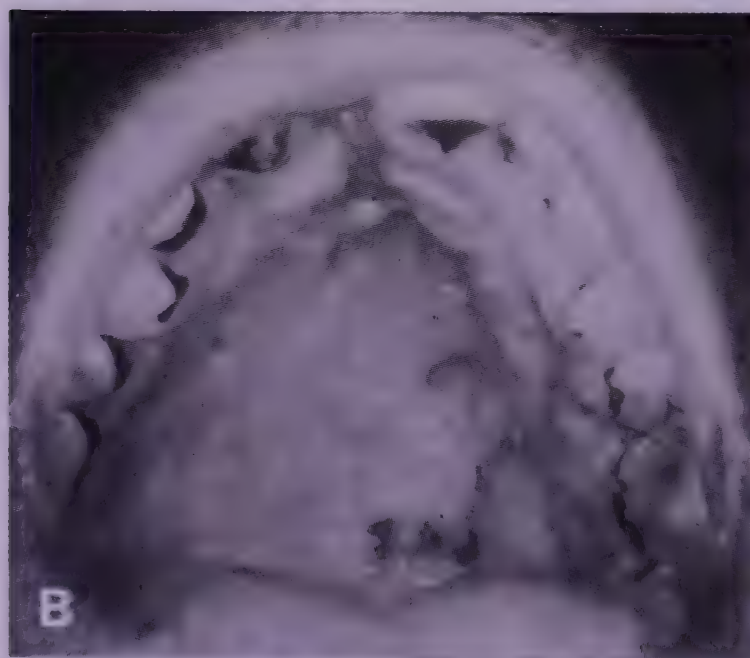
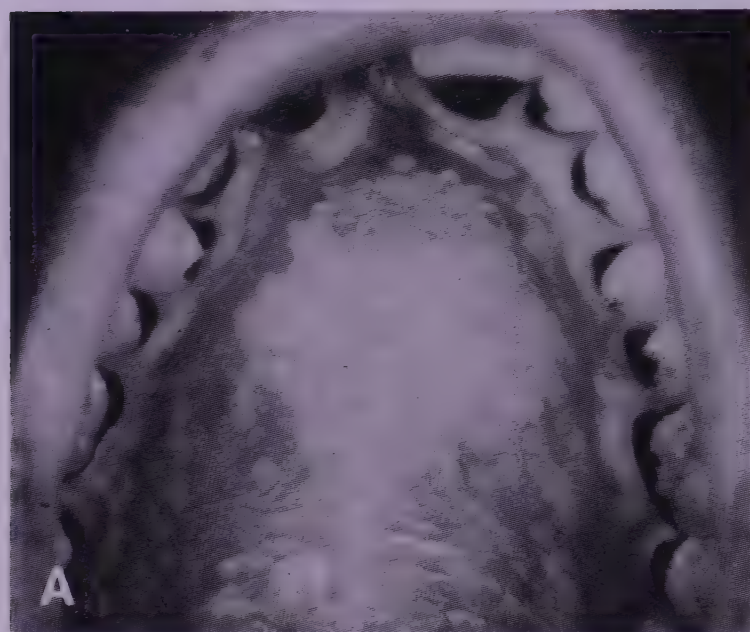


Fig. 4A. Palatal patch in a reverse smoker  
Fig. 4B. Cancer that developed four-years after observation of the patch seen in the Fig. 4A

Malignant transformation was observed for 0.3% of the palatal changes (Fig. 4A and B); however, it should also be noted that during the 10-year follow-up period in this area, 10 of the 11 oral cancers were palatal cancers and they arose from pre-existing palatal changes (9). In a 10-year intervention study in the same area (11), the malignant potential of various components of palatal changes was evaluated: red areas and patches were found to exhibit a high potential for malignant transformation (Table 2).

## DISCUSSION

Although reverse smoking is practised in various forms in different parts of the world (see paper by Pindborg *et al.*, this volume), its long-term effects have been studied extensively only in Srikakulam district. The present overview clearly shows that reverse *chutta* smoking is causally associated with palatal cancer and palatal changes. The palatal changes are pre-cancerous, and most palatal cancers originate from them. Of the several components of palatal changes, red areas and patches seemed to be most important from the point of view of cancer development. Although 25% of the excrescences showed dysplasia of the surface epithelium (10), none of the malignancies arose from excrescences. Excrescences showed higher regression rates, and it was demonstrated that they represent an initial reaction to reverse smoking and are transient.

Although reverse *chutta* smoking affected all parts of the oral mucosa, the effect was most striking on the palate, where most of the cancers and the precancerous changes occurred. The most common non-palatal site was the dorsum of the tongue, an area close to the lighted end of the *chutta*; one of the 11 cancers (9) among reverse smokers was on the dorsum — otherwise an uncommon intraoral location for cancer.

A pertinent question is about the role of heat from reverse smoking in the pathogenesis of palatal cancer. Palatal cancer and palatal



**Table 2**  
*Malignant transformation rates per 1000 for various palatal components*

Component	Reverse smokers			Conventional smokers		
	Components	Malignant transformation		Components	Malignant transformation	
	(no.)	No.	per 1000	(no.)	No.	per 1000
Keratoses	4111	—	—	656	—	—
Excrescences	3431	—	—	577	—	—
Patches	926	11	12	76	—	—
Red areas <sup>a</sup>	136	16	118	8	2	250
Ulcers	122	—	—	17	—	—

<sup>a</sup>In two individuals, patches turned to red areas before cancer developed

changes are also observed, although to a lesser extent, among conventional *chutta* smokers but are most common among reverse smokers. This may mean that heat plays an important role in the pathogenesis. Interestingly, application of *chutta* smoke condensate in acetone to the skin of Swiss mice and albino rats followed by exposure to heat resulted in skin cancers in 79% of the 14 animals. In contrast, none in an untreated group, a group treated with tobacco tar alone, a group given heat alone or a group given acetone alone developed cancers (1). The authors concluded that heat functions as a co-carcinogen and accelerates neoplastic change.

No reports have been made so far, on the treatment of palatal changes. Their

management currently consists of persuading smokers to give up their tobacco habits. Considering that reverse smoking is also associated with higher mortality rates from other diseases (12), its cessation would be most desirable and beneficial. Cessation of reverse smoking was also associated with a drop in the incidence rates of palatal changes (13) and this is an encouraging proposition for primary prevention.

### Acknowledgments

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# Oral health consequences of tobacco use in Ernakulam district, Kerala, India

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*Bidi* smoking and betel-quid (*pan*) chewing are the most common forms of tobacco use in Ernakulam district. They are strongly associated with oral cancer, various precancerous lesions and conditions, and others which do not seem precancerous. Nodular leukoplakia and submucous fibrosis are a very high-risk precancerous lesion and condition, respectively; other clinical types of leukoplakia also indicate a significant risk for oral cancer. Malignant transformation was not associated with leukoedema, leukokeratosis nicotina palati, palatal erythema, central papillary atrophy of the tongue, *pan*-chewer's lesion or oral lichen planus-like lesion. Most of these oral lesions remained stationary, some regressed and few recurred; submucous fibrosis, however, did not regress. Overall, tobacco use was found to influence the entire natural history of precancer, indicating the need to implement tobacco control measures.

## INTRODUCTION

Ernakulam district in the State of Kerala, is on the south-western coast of India. In 1966, at the time of initiation of our epidemiological studies, the district had an area of 3340 km<sup>2</sup> and a population of 1 859 913 (1961 census). *Bidi* smoking and betel-quid (*pan*) chewing are the main forms of tobacco use in this area (see paper by Bhonsle *et al.*, this volume). In this paper we describe the oral health consequences of these forms of tobacco use on the basis of various epidemiological studies conducted over the past 24 years.

## MATERIAL AND METHODS

Three main studies were conducted in Ernakulam district (Table 1). Phase 1 was a cross-sectional study among 10 287 villagers aged 15 years and over in 14 *karas* (*kara* is a smallest sampling unit) selected by random sampling (1). Some 59% of these individuals were tobacco users. Phase 2 was a 10-year

prospective study of those examined in phase 1 (2). Phase 3 was an intervention trial in a new sample of 12 212 tobacco users in 23 *karas* (3). It consisted of a base-line survey and a 10-year follow-up of these individuals. An additional survey was carried out among 5099 people in five *karas* in the Parakadavu area (4), and people with lesions and matched controls were followed-up annually.

Prior to examination, the frequency of tobacco use, i.e., the number of times per day

**Table 1**

*Main studies conducted in Ernakulam district*

Studies	Population (no.)	Tobacco users (%)
Phase 1 and 2 (1966-77)	10 287	59%
Phase 3 (1977-88)	12 212	100%
Parakadavu survey (1971)	5 099	55%



an individual smoked or chewed tobacco, the duration of such habits and other relevant details were recorded by trained interviewers. Examinations were conducted in a house-to-house approach, and selected oral lesions were recorded as per standardized criteria (1,5). All lesions were photographed in colour at the initial diagnosis and subsequently whenever necessary. Several hundred oral lesions were biopsied, and smears were obtained for cytological examination as per the requirement of the particular survey.

### LESIONS ENCOUNTERED

Almost all of the oral lesions were observed only among tobacco users. In this paper, the lesions can be grouped broadly as shown below on the basis of their frequency in groups with different habits.

**Predominantly associated with smoking:** (i) leukoedema; (ii) leukokeratosis nicotina palati; (iii) palatal erythema; and (iv) central papillary atrophy of the tongue

**Predominantly associated with chewing:** (i) *pan*-chewer's lesion; (ii) oral lichen planus-like lesion; and (iii) oral submucous fibrosis

**Associated with smoking and chewing (mixed habit):** (i) leukoplakia and preleukoplakia; (ii) oral lichen planus; and (iii) oral cancer

### LESIONS PREDOMINANTLY ASSOCIATED WITH SMOKING

As mentioned earlier, *bidi* smoking is the most popular smoking habit, especially among men in this area. Overall, 17% of the 10 287 individuals examined in phase I smoked *bidis* (1).

**Leukoedema:** This is a chronic mucosal condition in which the oral mucosa has a grey, opaque appearance (Fig. 1) as though a greyish film were hanging over it like a veil. When the mucosa is stretched the lesion disappears, only to reappear when it is relaxed.

**Epidemiology:** The prevalence of leukoedema was 0.4%. About 16 (62%) of the 26



Fig. 1. Leukoedema (L) in the buccal mucosa of a *bidi* smoker

leukoedemas were seen among *bidi* smokers and the rest in people who smoked and chewed (1). The annual age-adjusted incidence rate of this lesion was 2.5 per 1000; it was 3.8 per 1000 among smokers (2).

**Histological features:** Leukoedema was characterized by accumulation of spongy vacuolated cells in the superficial epithelial layer, ballooning cells in the stratum spinosum and epithelial hyperplasia (6).

**Natural history:** Of the 87 leukoedemas (includes incidence lesions) followed-up over a 10-year period, 64% remained stationary and 36% regressed; no malignant transformation was observed (2).

**Leukokeratosis nicotina palati:** This lesion which is commonly seen among conventional smokers, consists of a greyish-white palate with small nodular excrescences having small central red dots, corresponding to the inflamed orifices of the minor salivary glands (Fig. 2).

**Epidemiology:** The prevalence of this lesion was 0.3%; 52% of the 31 lesions occurred among *bidi* smokers (1). The annual age



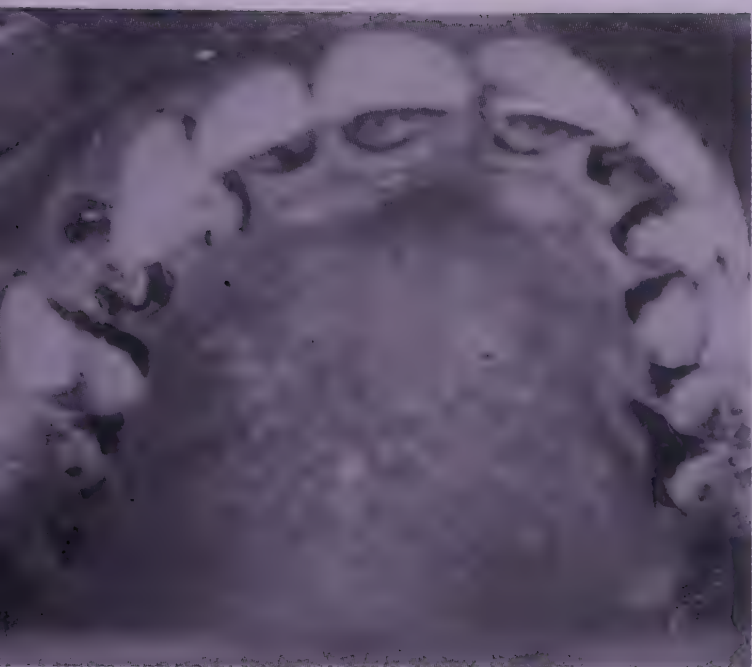


Fig. 2. Leukokeratosis nicotina palati in a *bidi* smoker

adjusted incidence rate among smokers was 1.7 per 1000; it was 0.7 per 1000 in those who smoked and chewed (2).

**Natural history:** Over a 10-year period, 66% of the 44 lesions remained stationary, 34% regressed spontaneously and none showed malignant transformation (2).

Leukokeratosis nicotina palati observed among conventional smokers must be distinguished from the palatal changes associated with reverse *chutta* smoking (see paper by Daftary *et al.*, this volume). Palatal changes in reverse smokers are multimorphic and precancerous, whereas leukokeratosis nicotina palati exhibits neither great variability nor malignant transformation.

**Palatal erythema:** Palatal erythema is marked by a diffused erythematous hard palate (Fig. 3A), occasionally extending to the soft palate.

**Epidemiology:** Of the 69 lesions observed among 7216 tobacco users (Table 2), 87% occurred among smokers, especially *bidi* smokers. This lesion was observed in only three women, which corresponds to the low prevalence of *bidi* smoking among women.

**Clinical aspects:** The lesion occurred either independently or sometimes with other lesions.

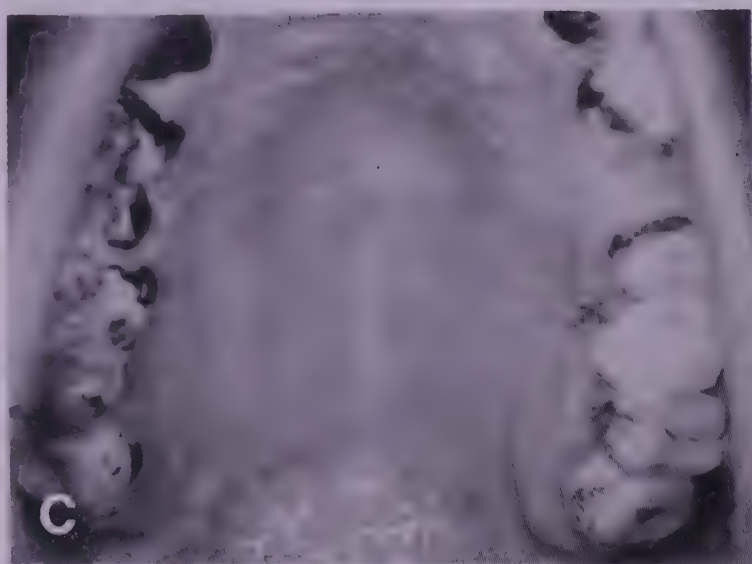
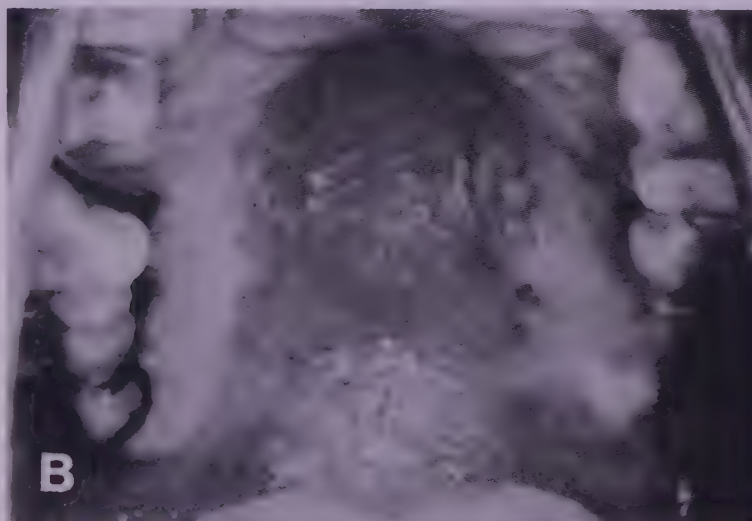
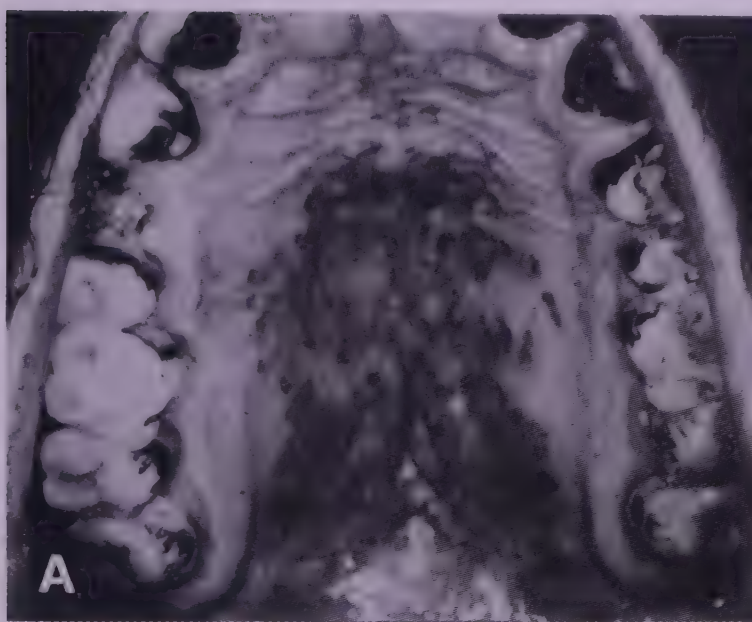


Fig. 3A. Palatal erythema in a *bidi* smoker

Fig. 3B. Palatal erythema with papillary hyperplasia in a *bidi* smoker

Fig. 3C. Regression of palatal erythema shown in Fig. 3A, following discontinuation of smoking; note loss of pigmentation



**Table 2**

*Distribution of individuals with palatal erythema according to habit and sex*

Habit	Men (n=6978)	Women (n=238)	Total (n=7216)
Smoking	58 (88%)	2 (67%)	60 (87%)
Smoking & chewing	8 (12%)	1 (33%)	9 (13%)
Total	66 (100%)	3 (100%)	69 (100%)

About 10% of the lesions were associated with palatal papillary hyperplasia (Fig. 3B) and 25% with central papillary atrophy of the tongue and bilateral commissural leukoplasias. This triad of lesions is comparable to the 'multifocal candidiasis' described in western literature (7).

**Natural history:** Over a 10-year period, 35% of the 69 lesions persisted, 56% regressed and 9% were transient, i.e., they regressed, recurred and regressed again (Table 3). Interestingly, the highest percentage (60%) of persistent lesions was seen among people who did not give up their smoking habits, while the highest percentage (75%) of regressed lesions occurred among those who discontinued or reduced smoking substantially (Fig. 3A and C). Most of the transient lesions were associated with inconsistent habit practices, i.e., among those who stopped their habits,

restarted and stopped. These observations clearly indicate that palatal erythema is caused by smoking, particularly *bidi* smoking.

**Central papillary atrophy of the tongue:** This lesion has also been described in the literature as median rhomboid glossitis and localized atrophy of the tongue papillae (1). It consists of a well-defined, oval, pink area in the centre of the dorsum of the tongue devoid of lingual papillae (Fig. 4A).

**Epidemiology:** The prevalence of this lesion was 1%; it was present among 2.2% *bidi* smokers, 1.6% cigarette smokers and 0.3% non-users of tobacco (1). In the 10-year follow-up study, the annual age-adjusted incidence rate among smokers was 1.5 per 1000 as compared to 0.8 per 1000 among nonsmokers (2).

**Etiology:** Central papillary atrophy of the tongue, is considered to be due to candidal infection, smoking or both (8). In this study, central papillary atrophy exhibited a strong association with smoking, particularly *bidi* smoking. This was exemplified by its higher prevalence (1) and incidence rates (2) among smokers, its long-term behaviour in relation to the cessation or reduction of smoking (see below) and the observation that 87% of the lesions occurred among *bidi* smokers (8). Interestingly, very few women had this lesion, due perhaps to the rarity of smoking among women.

**Table 3**

*Behaviour of palatal erythema according to change in tobacco use over a 10-year period*

Palatal erythema	Tobacco use							
	Unchanged/ increased		Reduced/ stopped		Not constant		Total	
	No.	%	No.	%	No.	%	No.	%
Persistent	15	60%	9	23%	—		24	35%
Regressed	9	36%	30	75%	—		39	56%
Transient	1	4%	1	2%	4	100%	6	9%
Total	25	100%	40	100%	4	100%	69	100%



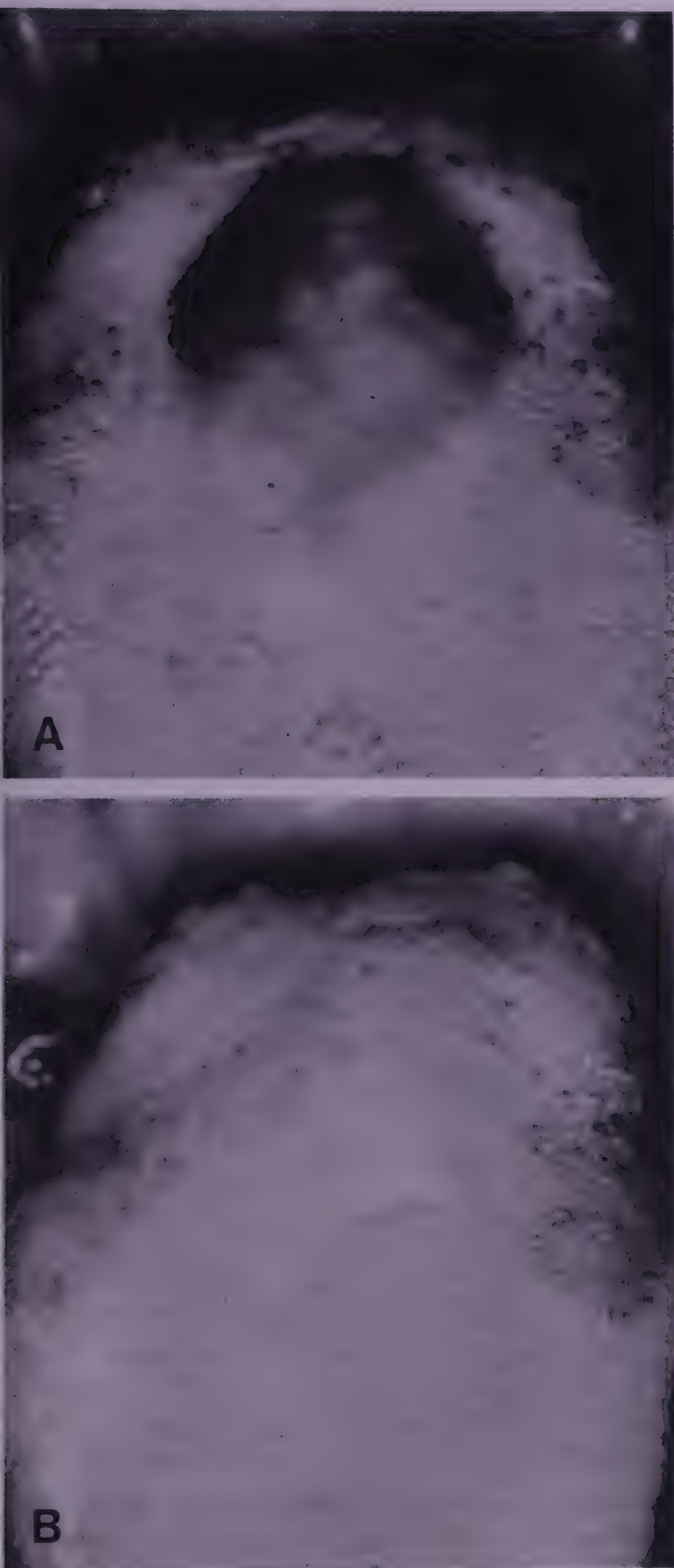


Fig. 4A. Central papillary atrophy of the tongue in a *bidi* smoker

Fig. 4B. Regression (repapillation) of the lesion shown in Fig. 4A following discontinuation of *bidi* smoking

**Clinical aspects:** Most of the 182 lesions studied were pink to dark-pink, oval or

elongated; some were rhomboid or irregular (8). The mean length was 2.7 cm and the breadth, 1.3 cm. They were generally smooth, but some were fissured. In 69% of cases the lesion occurred independently; 14% had co-existent palatal erythema and 8% had leukoplakia. A triad of central papillary atrophy, bilateral commissural leukoplakia and palatal erythema, comparable to the 'multifocal candidiasis' described in western literature (7) was seen in 3% of cases. The remaining occurred with other lesions. Central papillary atrophy of the tongue must be distinguished from the atrophic candidiasis reported among people with human immunodeficiency viral infection (9).

**Histological features:** This lesion was marked by the absence of tongue papillae, the presence of slight parakeratinization of the epithelial surface, long slender rete ridges and occasional pseudocarcinomatous hyperplasia. Chronic inflammatory cell infiltrate, chiefly of lymphocytes, was usually present within the epithelium and in the lamina propria. In a single periodic acid-Schiff section study of 12 biopsies, candidal hyphae were observed in 67% (8).

**Natural history:** Some 50% of the 182 lesions that were observed for 10 years were persistent (8), 43% regressed, i.e., repapillated, 5% regressed and recurred and 2% showed inconsistent behaviour (regressed, recurred and regressed). The highest percentage (65%) of persistent lesions was found among people who did not stop or reduce their habits, while the highest percentage (87%) of regressed lesions (Fig. 4A and B) was seen in those who stopped their habits. None of the lesions progressed to cancer.

### LESIONS PREDOMINANTLY ASSOCIATED WITH BETEL-QUID CHEWING

Tobacco was most often chewed as an ingredient in betel quid (*pan*) by 33% of the women



and 35% men in Ernakulam district (see paper by Bhonsle *et al.*, this volume). Betel-quid chewing inevitably stains the mucosa bright red, due to the formation of *o*-quinone from water-soluble polyphenols, notably, leucocynidins, at the alkaline pH of 8-9 *via* secondary reactions (10). These stains can be washed clean or disappear with abstinence from chewing; however, it is not unusual to see persons with perpetually stained mucosa.

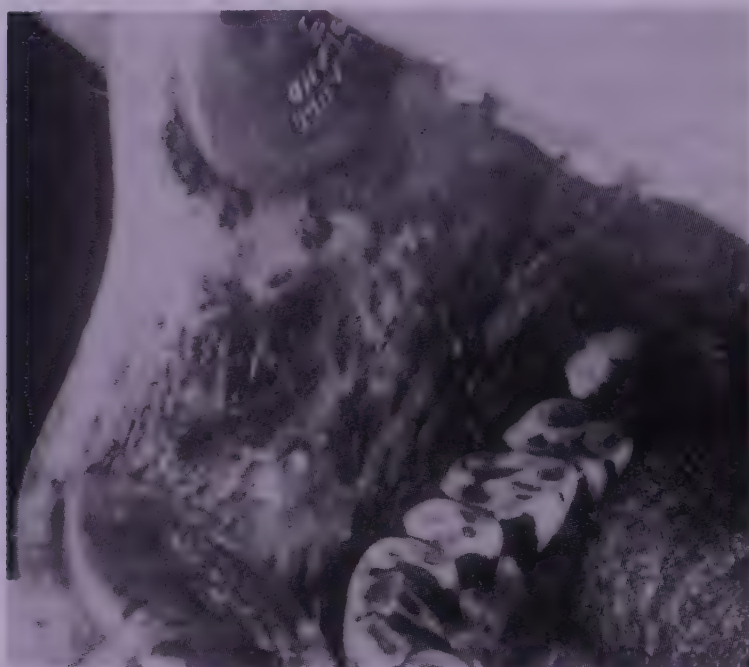


Fig. 5. *Pan*-chewer's lesion

***Pan-chewer's lesion:*** This lesion consists of a thick brownish-black encrustation on the buccal mucosa (Fig. 5) at the site of placement of the betel quid. It was often seen among heavily addicted betel-quid chewers. It could be scraped off with a piece of gauze; it regresses spontaneously, more frequently when the habit is discontinued.

***Epidemiology:*** The annual age-adjusted incidence rate of this lesion was 28 per 1000 among male chewers and 17.4 per 1000 among female chewers (2).

***Histological features:*** These lesions showed pale-staining parakeratin-like surface layers of epithelium, containing round nuclear remnants, ballooning and vacuolated cells and epithelial hyperplasia.

***Natural history:*** *Pan*-chewer's lesion is a specific entity and rarely progresses to leukoplakia. Over a three-year observation period, 26% of the 532 observed lesions were persistent, 45% regressed spontaneously and 29% recurred; malignant transformation was not observed in these lesions (2).

***Oral lichen planus-like lesion:*** A characteristic lesion consisting of white, wavy, parallel, non-elevated striae that do not crisscross (Fig. 6A) (as in lichen planus) was observed. Sometimes, these striae radiate from a central erythematous area (Fig. 6B) at the site of placement of the betel quid.

***Epidemiology:*** The prevalence of this lesion among 5099 individuals in Parakadavu was 0.7% (4). About 89% of the lesions occurred among betel-quid chewers and 11% among people with mixed habits. In a 10-year follow-up study of 10 000 villagers in Ernakulam district, the annual age-adjusted incidence rates among men and women were 0.7 and 2.2 per 1000, respectively (2). The peak incidence for women was in the 45-54-year age group. The incidence was zero among smokers and non-users of tobacco; 4.3 per 1000 among women who chewed. This lesion is thus entirely associated with betel-quid chewing.

***Clinical aspects:*** The striae seen in these lesions were very fine, like fingerprints, and always occurred in the buccal mucosa and mandibular groove, locations which are in intimate contact with the betel quid.

***Histological features:*** The lesion shows parakeratinized atrophic epithelium, liquifecation degeneration of the basal-cell layer and a band-like inflammatory cell infiltrate containing lymphocytes and plasma cells (4). Unlike lichen planus, this lesion shows hyperparakeratosis, and plasma cells in the juxtaepithelial region.

***Natural history:*** A total of 42 lesions were followed-up for four years; 79% remained stationary, 21% regressed and two of the



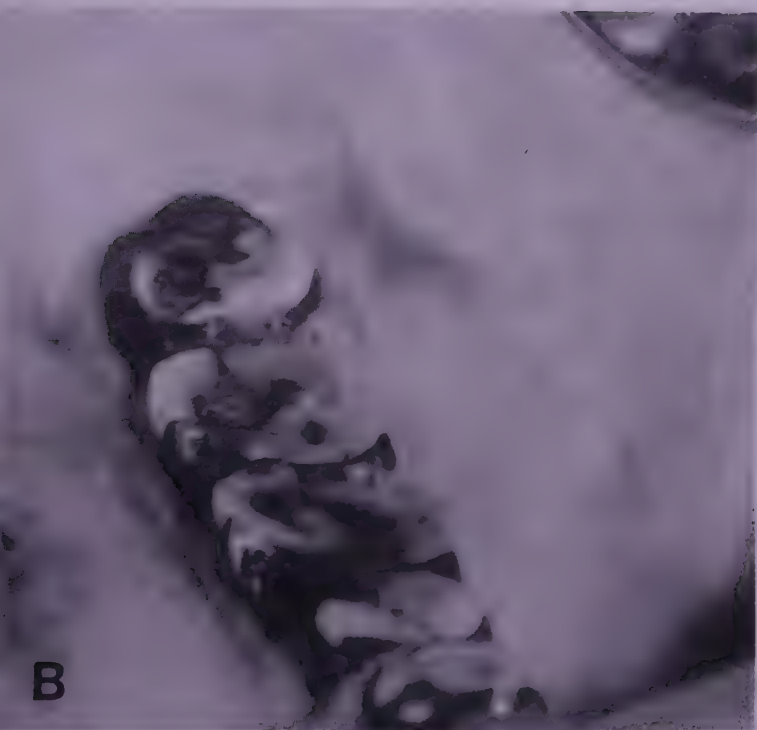


Fig. 6A. Oral lichen planus-like lesion in buccal mucosa

Fig. 6B. Radiating striae from a central erythematous area at the site of placement of betel quid

nine regressed lesions recurred (2). Although the histological features were similar to those of oral lichen planus, in view of its complete association with betel-quid chewing, it is regarded as a specific entity.

**Oral submucous fibrosis:** This is a chronic oral mucosal condition marked by rigidity of the mucosa of varying intensity (Fig. 7) due to fibro-elastic transformation of the juxta-epithelial layer, resulting in progressive inability to open the mouth (Fig. 8). When the tongue is involved, it is shrunken and hard (Fig. 9), with restricted mobility. Occasionally,



Fig. 7. Buccal mucosal involvement with blanching in oral submucous fibrosis

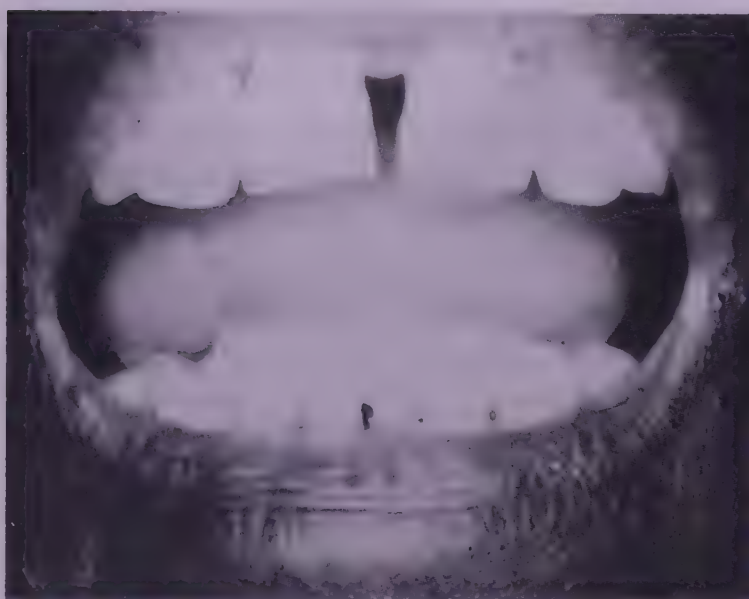


Fig. 8. Limited oral opening in submucous fibrosis; also shows shrunken tongue with impaired protrusion

pharyngeal and oesophageal involvement have also been observed. Submucous fibrosis occurs predominantly among Indians, Indians settled abroad and to a lesser extent in other Asiatics. Areca-nut (*Areca catechu*) chewing in any form is currently believed to be the primary etiological agent for this condition (11-13) (see also paper by Sinor *et al.*, this volume); areca nut is



an indispensable ingredient of betel quid (see paper by Bhonsle *et al.*, this volume).

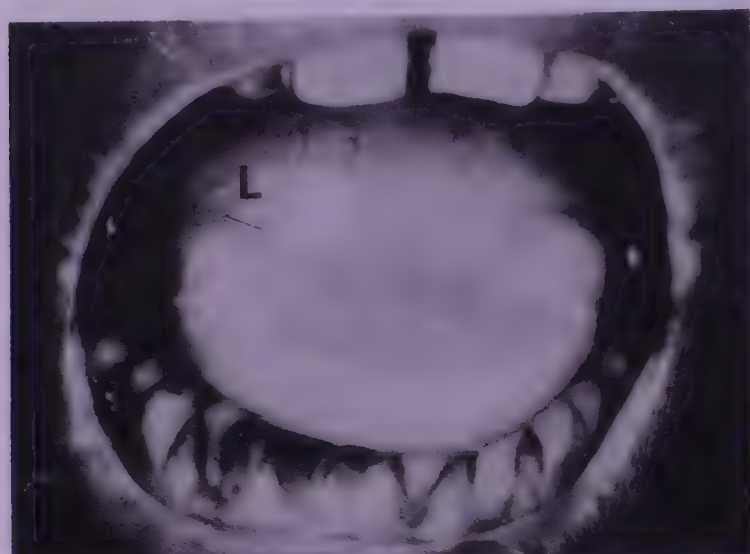


Fig. 9. Involvement of the tongue marked by absence of lingual papillae and restricted protrusion; note a homogeneous leukoplakia (L) on the dorsum and loss of pigmentation from the vermilion borders

**Epidemiology:** The prevalence (1,14) and the incidence (2) rates of submucous fibrosis are high in Ernakulam district as compared to other areas of India. The overall prevalence was 351 per 100 000; it was highest (1090 per 100 000) among betel-quid chewers (Table 4). The annual age-adjusted incidence rate was 7 per 100 000 among men and 17 per 100 000 among women (2); all new cases occurred among betel-quid chewers. The prevalence rates seem to be too high in comparison with the incidence rates because this condition does not regress like other precancerous lesions.

**Clinical aspects:** Submucous fibrosis affects people of each sex, but a definite female predominance was observed in Ernakulam (2,14), which was related to the extent of areca-nut (betel-quid) chewing (12). For example, in this area, most of the betel-quid chewers were women, so there were more women with this condition. Submucous fibrosis occurs in the age range 20-40 years, with some regional variation; for instance, the mean age of individuals with this condition in Pune was lower (37 years) than that in Ernakulam (51 years)

**Table 4**  
*Prevalence of oral submucous fibrosis according to tobacco habit<sup>a</sup>*

Habit	No. examined	Prevalence	
		No.	Per 100 000
No habit	4 210	2 <sup>b</sup>	48
Smoking	2 272	—	—
Chewing	2 661 <sup>c</sup>	29	1090
Mixed	1 106	5	452
Total	10 249	36	351

<sup>a</sup>Source: ref. (1)

<sup>b</sup>Past chewers

<sup>c</sup>38 individuals who chewed *pan* without tobacco not included

(12). The age of individuals with this condition may also depend on the type of areca-nut chewing habit and the age at initiation of the habit.

Submucous fibrosis commonly affects the buccal mucosa (Fig. 7), retromolar areas and soft palate. The frequency of their involvement varies, however, with geographic area, depending on the type of areca-nut chewing (12). The earliest and commonest sign of this condition is blanching (15), which imparts a marble-like appearance to the mucosa. When the disease is fully developed, palpable fibrous bands develop in the buccal mucosa, soft palate and rima oris; they run vertically in the buccal mucosa and are circular around the rima oris. As the disease progresses, the mucosa becomes stiff and the oral opening may be restricted. Petechial spots resulting from the breakdown of connective-tissue support of the vasculature were observed in 11% of cases in one study (16). Submucous fibrosis is often associated with leukoplakia (Fig. 9), oral cancer and pigmentation changes (14). Most patients complain of a burning sensation, often aggravated by spicy food and excessive or decreased salivation.

**Histological features:** The most common histological features of this condition are



epithelial atrophy with juxtaepithelial hyalinization and collagen of varying density. A notable feature was the presence of epithelial dysplasia in 26% of cases (17).

**Natural history:** Unlike other precancerous lesions, submucous fibrosis does not regress, either spontaneously or with discontinuation of the habit. The most serious aspect of this condition is its precancerous nature (18). In a 17-year follow-up of 66 cases, oral cancer had developed in 0.4% of cases at the end of 10 years (2), 4.5% at the end of 15 years (17) and 7.6% at the end of 17 years (19). In an eight-year follow-up study of 25 cases, the relative risk of malignant transformation for submucous fibrosis, compared to that of tobacco users without any oral mucosal lesion or condition, was 397.3 (20).

**Primary prevention:** As mentioned above areca-nut chewing in any form is involved in the pathogenesis of this condition. There is no effective cure, so far, for this condition. Discontinuation of all forms of areca-nut and tobacco use would probably limit the extension of this disease and prevent malignant transformation. Stoppage of betel-quid chewing would probably lead to a decrease in the incidence of submucous fibrosis (21). This approach assumes great importance in view of the upsurge in *mawa* and *pan masala* usage in the country (see papers by Bhonsle *et al.*; Sinor *et al.*, this volume).

## LESIONS ASSOCIATED WITH SMOKING AND CHEWING

The combined habit of smoking as well as chewing tobacco, mostly in betel quid (*pan*), was practised overall by 11% of the 10 287 individuals (1); almost all of them were men.

**Leukoplakia:** Leukoplakia, literally means a white patch. It was hypothesized initially as precancerous mainly because of its co-existence with oral cancer; it has a similar intraoral location as that of oral cancer. Leukoplakia is defined as a raised white patch

of oral mucosa measuring 5 mm or more, which cannot be scraped off and which cannot be attributed to any other diagnosable disease. This definition does not carry any histological connotation (5).

**Epidemiology:** The prevalence of this lesion in Ernakulam district was 17 per 1000; it was highest (61 per 1000) among people with mixed habits (Table 5). The annual age-adjusted incidence rate was 2.1 per 1000 among men and 1.3 per 1000 among women; the highest incidence (6.0 per 1000) was among men who both chewed and smoked (2).

**Table 5**

*Prevalence of leukoplakia according to tobacco habit<sup>a</sup>*

Habit	Total no.	Prevalence	
		No.	per 1000
No habit	4 210	8	2
Smoking	2 272	48	21
Chewing	2 661 <sup>b</sup>	47	18
Mixed	1 106	67	61
Total	10 249	170	17

<sup>a</sup>Source: ref. (1)

<sup>b</sup>38 individuals who chewed *pan* without tobacco not included

Almost all leukoplakias in India occur in tobacco users. A definite dose-response relationship between leukoplakia and various forms of tobacco use in this area has been demonstrated (22). The dose-response relationship was stronger for smoking habit than for the chewing habit and remained significant after taking account of age, sex and type of tobacco habit.

**Clinical aspects:** Leukoplakias are classified into (i) homogeneous; (ii) ulcerated; and (iii) nodular types (5). Homogeneous leukoplakia is characterized by a raised formation of plaques or groups of plaques varying in size, with irregular edges (Fig. 10A). The lesions are predominantly white but may also be



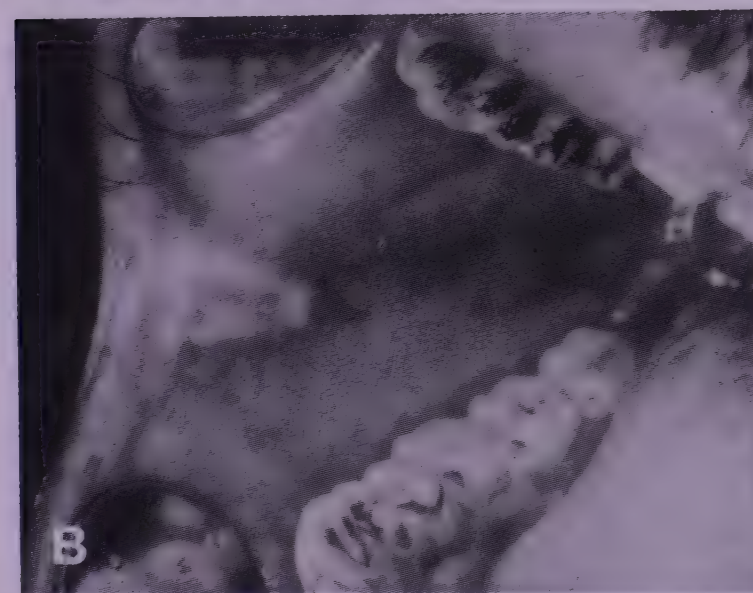
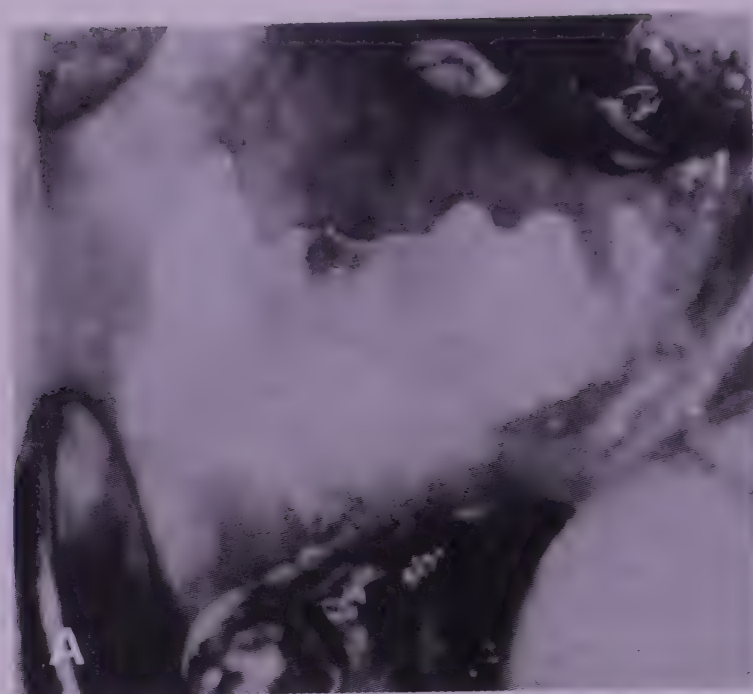


Fig. 10A. Homogeneous leukoplakia

Fig. 10B. Ulcerated leukoplakia

Fig. 10C. Nodular leukoplakia

greyish-yellow. Ulcerated leukoplakia consists of an area of ulceration sometimes surrounded by keratinized areas, pigmentation or both (Fig. 10B). Nodular leukoplakia shows many small white nodules on a erythematous base (Fig. 10C). Some 75% of the leukoplakias in this region were homogeneous, 20% ulcerated and 5% nodular leukoplakias (5). The risk for cancer varies with clinical type of leukoplakia (Table 6).

Leukoplakias occur from the age of 20 onwards. For men, the incidence increases steadily from the age of 20; for women, however, the peak incidence is in the age range 50-60 years, after which there is a drop (2). Most (88%) leukoplakias are located on the buccal mucosa, commissures and tongue (5). Ulcerated leukoplakias are associated with *bidi* smoking and are generally located in the commissures, whereas homogeneous leukoplakias associated with *bidi* smoking occur on the commissures and anterior part of the buccal mucosa; those associated with betel-quid chewing and mixed habits are often situated on the posterior part of the buccal mucosa. As mentioned above, in some instances commissural leukoplakias among *bidi* smokers occurred with palatal erythema and central papillary atrophy of the tongue, a triad comparable to the 'multifocal candidiasis' reported in western literature (7).

**Histological features:** Leukoplakias associated with betel-quid chewing showed hyperorthokeratosis in 82% and hyperparakeratosis in 12%; those associated with mixed habits of smoking and chewing showed hyperorthokeratosis in 63% and hyperparakeratosis in 23% (1). Overall, epithelial dysplasia was observed in 8%; nodular leukoplakias accounted for 71% of dysplastic leukoplakias. In a study of 723 leukoplakias in different areas of India, 14% showed superimposed candidal hyphae (23); nodular leukoplakias showed the highest frequency of candidal hyphae.

**Natural history:** Of the 225 leukoplakias studied over a 10-year period, cancer developed



Table 6

*Relative risk for malignancy associated with various precancerous lesions and conditions<sup>a</sup>*

Precursor lesion/ condition	Total no.	Average follow-up period (years)	No. of oral cancers	Transformation per 100 000 per year	Relative risk
Nodular leukoplakia	13	2.8	6	16 216.2	3243.2
Submucous fibrosis	25	6.0	3	1 986.7	397.3
Others <sup>b</sup>	26	2.6	1 <sup>c</sup>	1 515.2	303.0
Ulcerated leukoplakia	105	4.4	1	218.8	43.8
Homogeneous leukoplakia	489	4.8	3	128.1	25.6
Lichen planus	344	3.7	1	78.9	15.8
None of the above	10 145	7.8	4	5.0	1.0

<sup>a</sup>Source: ref. (20)<sup>b</sup>Includes nonspecific diagnoses, such as red area, ulcers and benign growth<sup>c</sup>Preceding lesion, red area

in 4% cases, 47% remained stationary, 42% regressed and 7% recurred (2).

Malignant transformation was most frequent (21%) in nodular leukoplakias (Fig. 11A and B), as compared to 2% in homogeneous leukoplakia (2). In another study (Table 6), nodular leukoplakia showed the highest relative risk (3243.2) among all precancerous lesions and conditions for developing into oral cancer, as compared to the risk for people with tobacco habits but no oral lesion.

**Preleukoplakia:** This lesion can be considered a precursor lesion to leukoplakia. It consists of a low-grade or very mild reaction of the mucosa, appearing as a grey or greyish-white but never completely white area with a slight lobular pattern and indistinct borders blending into the adjacent normal mucosa (5). The prevalence of this lesion was 2.4%; it was seen more often among people who chewed and smoked (5). The annual age-adjusted incidence rate was 3.1 per 1000 among men and 0.2 among women; the incidence was highest (5.6 per 1000) among men who smoked and chewed (2); of the 309 preleukoplakias followed-up over a 10-year period, 15% progressed to leukoplakia and two cases to cancer.

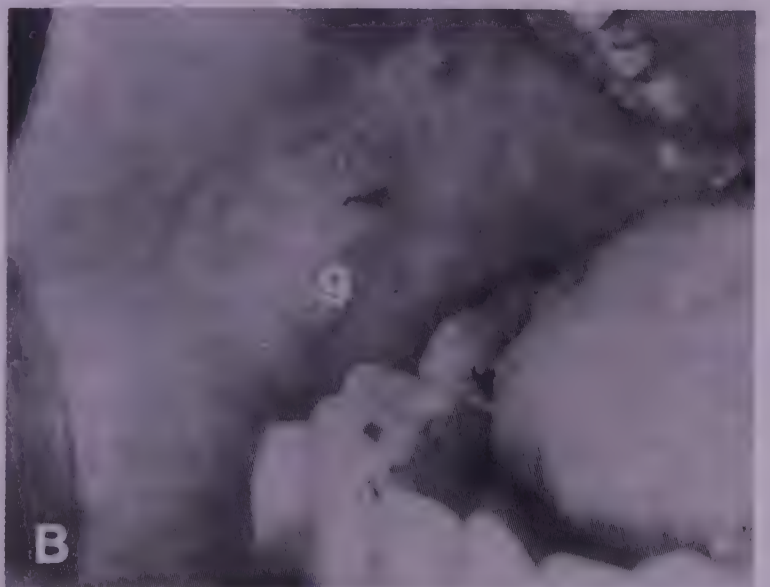
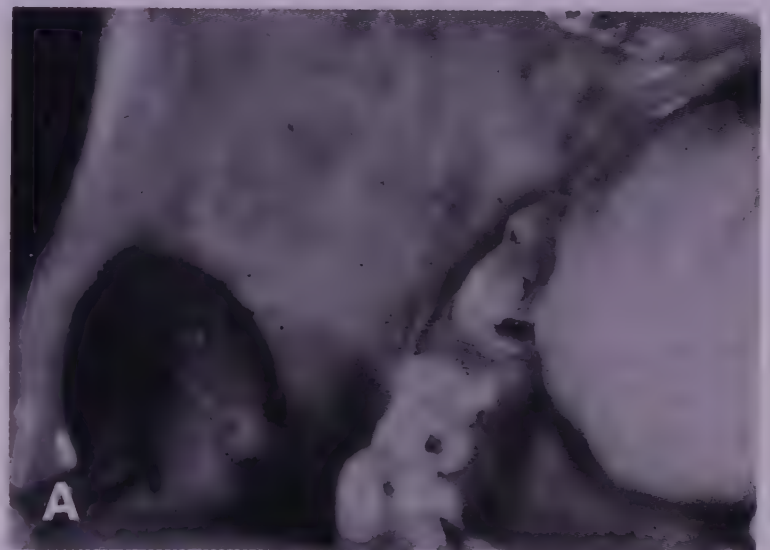


Fig. 11A. Nodular leukoplakia in the buccal mucosa

Fig. 11B. Exophytic growth (g) that developed in the lesion shown in Fig. 11A



**Oral lichen planus:** Oral lichen planus is primarily a dermatological disorder. Various mucosal surfaces may be involved in this condition, either independently, concurrently with cutaneous involvement or serially. Oral mucosa, however, is, more frequently affected mucosal location. Oral lesions are suspected to possess some cancer potential. Interestingly, in our study oral lichen planus was found to be strongly associated with tobacco habits.

**Epidemiology:** The overall prevalence of oral lichen planus was 1.5%; it was highest (3.7%) in those people with mixed habits and lowest (0.3%) in nonusers of tobacco (24). The annual age-adjusted incidence rate was 2.1 and 2.5 per 1000 among men and women, respectively. It was highest (8.2 per 1000) among men who smoked as well as chewed tobacco; among women it was highest (4.5 per 1000) in chewers (2). The relative risk for oral lichen planus was highest (13.7) among those who smoked and chewed tobacco (25).

**Clinical aspects:** Oral lesions are diagnosed on the basis of presence of Wickham's striae. Oral lichen planus occurred predominantly among women. The buccal mucosa was the most favoured location. Oral lichen planus occurred in diverse morphological forms such as reticular, annular, linear, erosive or ulcerated and pigmented forms; of these, 20% were erosive or ulcerated lesions (24) and about 11% were associated with pigmentation (26).

**Histological features:** Sixty lesions were studied microscopically and epithelial atrophy was observed in 82%, hyperortho or hyperparakeratosis in 90%, and Civatte bodies in 78%. Band-like juxtaepithelial inflammatory cell infiltrate was present in all biopsies (24).

**Natural history:** Most oral lesions persisted; some regressed and recurred. The regression rates were highest in nonusers of tobacco and lowest in people with mixed habits (2). The malignant potential of this condition was assessed in 722 affected individuals (27): over a

10-year period (mean, 5.1 years), oral cancer developed in three patients (0.4%) who had erosive (atrophic) lesions; all of them used tobacco. In an eight-year follow-up study of 344 individuals with oral lichen planus (20), the relative risk for malignant transformation was 15.8 (Table 6); this, did not, however, attain the 5% significance level. Overall, the high prevalence and incidence rates among tobacco users as well as its natural history strongly support the hypothesis that tobacco does play an important role in this condition.

**Oral cancer:** The term oral cancer is used in this paper to denote squamous-cell carcinoma, which comprises over 95% of all oral malignancies in Kerala. This disease is the most serious oral health consequence of tobacco use. Earlier hospital-based studies showed oral cancer to be the most frequent cancer in Kerala (28,29). More recent data from the National Cancer Registry show that among all cancers, oral cancer ranks first and third among men and women, respectively (30).

**Epidemiology:** In a cross-sectional study of 10 287 individuals in Ernakulam district, 12 oral cancers were diagnosed (117 per 100 000) (1); six were diagnosed among 2661 (225 per 100 000) betel-quid chewers and six among 1106 (542 per 100 000) with mixed habits. Although there was a substantial number of (4210) nonusers of tobacco and (2272) *bidi* smokers in this study, no oral cancer occurred among them.

In a 10-year follow-up study of 10 000 individuals, the annual-age adjusted incidence rate of oral cancer was 16 per 100 000; the incidence was highest (32 per 100 000) among people with mixed habits (2). Interestingly, although there were substantial person-years of observation, none of the cancers occurred among nonusers of tobacco or *bidi* smokers. The average age of *bidi* smokers in this study was low (31.2 years), as compared to 52.1 years for male chewers, and 43.8 years for males who smoked and chewed (1); this





Fig. 12. Exophytic squamous-cell carcinoma in the buccal mucosa with an associated leukoplakia

perhaps explains the absence of oral cancers among *bidi* smokers. Tobacco chewing and smoking are recognized as causal factors for oral cancer (31-33). Thus, the occurrence of oral cancer exclusively among tobacco users in Ernakulam substantiates the hazardous nature of tobacco.

**Clinical aspects:** Oral cancer is predominantly a disease of the elderly. For example, the average age of oral cancer patients, although based on small numbers, was 55 years (1). The age-specific incidence rates (2) showed that the peak occurrence of 57 per 100 000 per year was among people aged 55 years and above.

Oral cancer occurred more often among men. The buccal mucosa was the most frequently involved location in this region, and it often co-existed with leukoplakia (Fig. 12) or submucous fibrosis; it mostly arose from a

precancerous lesion or condition (2,20). In a 10-year follow-up study, all 12 oral cancers developed from precancerous lesions or conditions (2), while in an eight-year follow-up study (20), 15 of the 19 oral cancers developed from precancer, giving a relative risk of 69.2. The relative risks for oral cancer associated with various precancerous lesions were significant for nodular leukoplakia, submucous fibrosis and others, including red area, ulcerations and ulcerated and homogeneous leukoplakia. The risk was not significant for lichen planus (Table 6).

## POSSIBLE SOLUTIONS

This overview demonstrates that *bidi* smoking and betel-quid chewing are detrimental to oral health, as they are strongly associated with oral cancer, precancerous lesions and other mucosal pathologies. In view of these findings, specific studies for primary and secondary prevention were undertaken. Primary prevention was found to be feasible and effective (3,34,35) (see also paper by Gupta *et al.*, this volume). In the above-cited studies, oral examinations were conducted by dentists in a research set-up. The possibility of early detection of oral cancer by paramedical personnel in the governmental health care infrastructure was also explored in this area (36), and the results were encouraging (see paper by Mehta, this volume).

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# ***Mawa* chewing and oral submucous fibrosis in Bhavnagar, Gujarat, India**

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*Mawa* is an areca-nut preparation containing tobacco and lime. Its use is very popular among the youth in Bhavnagar. Recently, there has been an increased occurrence of submucous fibrosis in this area. A case-control study on submucous fibrosis in Bhavnagar showed a relative risk of 109.6 for all forms of areca-nut use, 106.4 for *mawa* chewing and 780.0 for chewing *mawa* as well as betel quid (*pan*). The relative risks increased with the increase in the duration and frequency of areca-nut chewing; a bivariate analysis also showed a multiplicative effect. Clinically, submucous fibrosis in Bhavnagar differed in regard to age, sex and location distribution from cases in Ernakulam. These variations could be due to the differences in the type of areca-nut chewing in these areas — *mawa* chewing in Bhavnagar and betel-quid chewing in Ernakulam. The findings raise several research questions and indicate a need for public health measures against areca-nut containing products.

## **INTRODUCTION**

Submucous fibrosis is a precancerous condition. The malignant potential of this condition is due to the atrophic epithelium that is often seen in submucous fibrosis and the action of carcinogens in tobacco upon it (1). Several factors, namely, the use of chillies (*Capsicum annum* and *Capsicum frutescens*) and nutritional deficiency states, were thought to be involved in its pathogenesis. Current epidemiological evidence highlights areca-nut (*Areca catechu*) chewing as an etiological factor in this condition (2-4).

A marked increase in the occurrence of submucous fibrosis has been seen recently, especially among the young, in Bhavnagar, Gujarat. This increase corresponds to the increasing popularity of *mawa* chewing in the population, especially among the youth. *Mawa* is a preparation containing thin shavings of areca nut with the addition of some tobacco

and slaked lime (see paper by Bhonsle *et al.*, this volume). A case-control study was conducted to investigate the association between *mawa* and other forms of areca-nut chewing and oral submucous fibrosis (5). In this paper we describe some of the findings from that study and the differences in the clinical characteristics of the disease associated with *mawa* chewing in Bhavnagar and that with betel-quid (*pan*) chewing in Ernakulam district, Kerala.

## **MATERIAL AND METHODS**

Submucous fibrosis was diagnosed on the basis of the presence of palpable fibrous bands, as per the standardized criteria (6) (see paper by Murti *et al.*, this volume). The case-control study was conducted in a dental clinic in Bhavnagar among 60 consecutive dental patients diagnosed with submucous fibrosis. Controls matched for age, sex, religion and



socioeconomic status were selected from among patients attending the same clinic who showed no evidence of oral submucous fibrosis or any other tobacco-associated oral mucosal lesion or condition. Prior to their examination, information on the type of areca-nut chewing, forms of tobacco use and other relevant information was recorded. All cases were photographed in colour.

The clinical features recorded in Bhavnagar were compared with those of 64 cases of submucous fibrosis reported earlier (3) from various population-based studies in Ernakulam district, which is about 2000 km south of Bhavnagar.

## RESULTS

An overwhelming majority (97%) of the 60 individuals with submucous fibrosis in Bhavnagar were men; some 79% of these were under the age of 35 years.

There were no marked differences in the smoking habits between the cases and controls, implying that smoking is not an etiological agent in this condition.

Table 1 gives the relative risks for different types of areca-nut chewing habits. All cases

occurred among people who were regular chewers of areca nut in one form or another, except one who was an occasional chewer. The overall relative risks were 109.6 for areca-nut chewing, 106.4 for *mawa* chewing and 780.0 for chewing *mawa* and betel quid.

Table 2 gives the relationship between the duration of chewing and its frequency per day. The relative risks increased with duration and frequency of the habits.

Table 3 shows the results of a bivariate analysis of the dose-response relationship according to duration and frequency. A multiplicative effect between duration and frequency of the chewing is clearly seen.

Table 4 shows the age and sex distribution of submucous fibrosis cases in both areas. Most of the (79%) individuals in Bhavnagar were in the age range 15-34 years, while in Ernakulam 94% were aged 35 years and over. This condition occurred overwhelmingly (97%) among men in Bhavnagar, whereas only 18% of cases were in men in Ernakulam.

Table 5 shows the location of submucous fibrosis in the mouth in the two areas. The buccal mucosa was affected more or less

**Table 1**  
*Association of submucous fibrosis with chewing habits<sup>a</sup>*

Chewing habits	Cases		Controls		Relative risk
	No.	%	No.	%	
No habit	1 <sup>b</sup>	2%	39	65%	1.0
Areca nut (no <i>mawa</i> ) <sup>c</sup>	5	8%	7	12%	29.9**
Areca nut (no tobacco) <sup>d</sup>	4	7%	2	3%	78.0**
<i>Mawa</i>	30	50%	11	18%	106.4**
<i>Mawa</i> (with others) <sup>e</sup>	20	33%	1	2%	780.0**
Overall	60	100%	60	100%	109.6**

<sup>a</sup>Source: ref. (5)

<sup>b</sup>Occasional areca-nut chewer

<sup>c</sup>Betel quid with tobacco; betel quid without tobacco + tobacco-lime

\*\* $p < 0.01$

<sup>d</sup>Including betel quid without tobacco

<sup>e</sup>Mostly betel quid with tobacco



**Table 2***Relationship between duration of chewing (in years), frequency of chewing (per day) and occurrence of submucous fibrosis<sup>a</sup>*

Chewing habit	Cases		Controls		Relative risk
	No.	%	No.	%	
<b>Duration (in years)</b>					
1-5	17	29%	10	47%	1.0
6-10	16	27%	5	24%	1.9
≥11	26	44%	6	29%	2.5
<b>Frequency (per day)</b>					
1-5	16	27%	10	47%	1.0
6-15	37	63%	10	48%	2.3
≥16	6	10%	1	5%	3.8
Total	59	100%	21	100%	

<sup>a</sup>Source: ref. (5)**Table 3***Dose-response relationship between chewing habits and submucous fibrosis<sup>a</sup>*

Frequency of chewing (per day)	Duration of chewing					
	≤5 years			>5 years		
	Cases	Controls	RR	Cases	Controls	RR
≤5	7	6	1.0	10	4	2.1
>5	11	4	2.3	33	7	4.0

<sup>a</sup>Source: ref. (5)**Table 4***Age and sex distribution of submucous fibrosis patients in Bhavnagar and Ernakulam districts*

Age (years)	Bhavnagar	Ernakulam <sup>a</sup>
15-24	13 (22%)	—
25-34	34 (57%)	4 (6%)
35-44	10 (17%)	17 (27%)
≥45	3 (5%)	43 (67%)
Mean age	29.1	51
<b>Sex</b>		
Men	58 (97%)	18 (28%)
Women	2 (3%)	46 (76%)
Total	60 (100%)	64 (100%)

<sup>a</sup>Source: ref. (3)

equally in both areas, but its involvement in Bhavnagar was generally restricted to the posterior one-third (Fig. 1). In Ernakulam, there was a more generalized involvement of the buccal mucosa. The disease was clinically advanced in Bhavnagar and less severe in Ernakulam. Retromolar areas (100%), soft palate (95%) and the uvula (55%) were very frequently affected in Bhavnagar (Fig. 2), but less frequently in Ernakulam. The tongue and the floor of the mouth were involved in 59% and 22%, respectively, in Ernakulam, whereas in Bhavnagar they were either not involved or the involvement was negligible.

Seven individuals with this condition in Bhavnagar were siblings from three families. No similar observation was made in Ernakulam district.

**Table 5**  
*Location distribution of submucous fibrosis in Bhavnagar and Ernakulam districts*

Location	Bhavnagar (n=60)		Ernakulam <sup>a</sup> (n=64)	
	No.	%	No.	%
Labial mucosa	30	50%	41	64%
Buccal mucosa	59	98%	62	97%
Retromolar area*	60	100%	14	22%
Hard palate*	—		12	19%
Soft palate*	57	95%	8	12%
Uvula*	33	55%	5	8%
Tongue*	1	2%	38	59%
Floor of the mouth*	—		14	22%

<sup>a</sup>Source: ref. (3)

\* $p < 0.01$

## DISCUSSION

This paper demonstrates that *mawa* and areca-nut chewing in various forms are strongly associated with the occurrence of submucous fibrosis in Bhavnagar and that this disease exhibits specific regional variations in its clinical characteristics.

The upsurge of the *mawa* habit is a recent phenomenon in Bhavnagar. This habit, with some minor variations and under different names, is widely prevalent in other parts of Gujarat and also elsewhere in India. The high relative risks for different areca-nut chewing groups, observed for the first time, are consistent with other epidemiological observations which implicate areca-nut chewing in the pathogenesis of this condition. For example, Bhonsle *et al.* demonstrated in a review that 34-100% of individuals with submucous fibrosis chewed areca-nut in various forms (3). This habit was observed to be much more prevalent among the cases than in the general population (2), and the prevalence (7) and the incidence rates (8) were higher among areca-nut (betel-quid) chewers (see paper by Murti *et al.*, this volume). In the present study, chewing areca-nut alone, i.e., *supari* (see paper by Bhonsle *et al.*, this volume), was observed

in 8% of cases in Bhavnagar; but this habit was practised by 67% of submucous fibrosis patients in Pune reported in an earlier study (3).

The above observations demonstrated a strong association of this condition with areca-nut chewing; similarly, a 10-year prospective intervention study showed a fall in the incidence of submucous fibrosis (4). In this study the annual incidence per 100 000 dropped from 21.3 among men and 45.7 among women in the control cohort to 8 and 29 in the intervention cohort, respectively. These findings also support the etiological role of areca-nut chewing in this condition.

It has been suggested that there might be a genetic susceptibility to areca-nut alkaloids and tannins in individuals with this disease (9,10). In this context, it must be noted that seven individuals with this condition were siblings from three families, sharing perhaps the same genetic predisposition and similar exposure to areca-nut chewing.

Submucous fibrosis exhibits notable regional differences in its age and sex distribution and its clinical characteristics; such variations are attributable to differences in





Fig. 1. Involvement of posterior one-third of the buccal mucosa and retromolar area in a *mawa* chewer

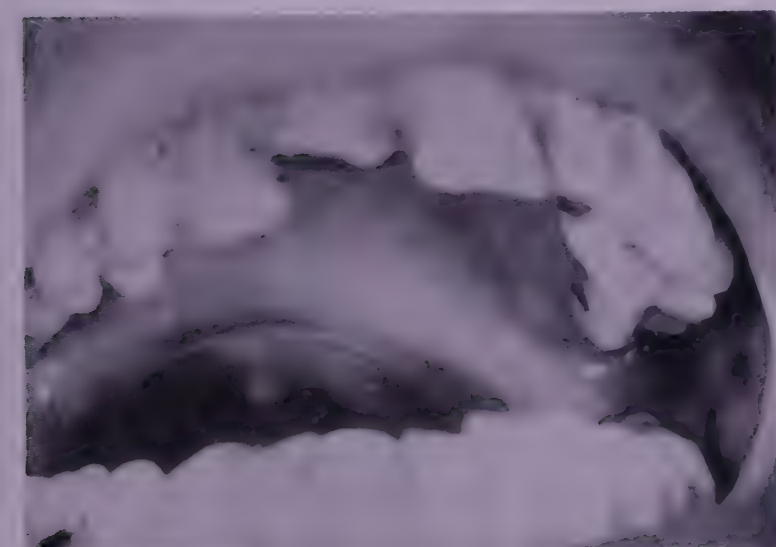


Fig. 2. Involvement of retromolar areas, soft palate and the uvula in a *mawa* chewer

areca-nut chewing practices in different areas (3). Similar observations were made in this investigation. The contiguous involvement of the posterior one-third of the buccal mucosa, retromolar areas (Fig. 1), soft palate and uvula (Fig. 2) in Bhavnagar could be due to the habit of keeping the *mawa* quid in the posterior part of the mandibular groove. In Ernakulam, exposure of the buccal mucosa to the betel quid is generalized; this may be responsible for the more diffuse involvement of the buccal mucosa.

Long-term studies on malignant transformation rates of submucous fibrosis among betel-quid chewers show that (see paper by Murti *et al.*, this volume) the mean age (51 years) of individuals with this condition in Ernakulam was higher than that in Bhavnagar (29 years). Correspondingly, the mean age of individuals with this condition who developed oral cancer (7.6%) in Ernakulam was 64.6 years (11). In view of the very low mean age (29 years) of the patients in Bhavnagar, it would be important to find out whether they develop oral cancer at an earlier age. It would also be important to know whether submucous fibrosis among areca-nut chewers with no concurrent tobacco use develops into oral cancer.

The health hazards of tobacco use are well recognized; consequently, tobacco control measures are receiving priority. While epidemiological studies have revealed no significant risk for oral cancer associated with areca-nut chewing (12), this habit certainly appears to be involved in the pathogenesis of oral submucous fibrosis, which is itself often a progressive disease with a burning sensation and dryness of the mucosa, with no effective cure. Furthermore, a recent study demonstrated a high relative risk (397.3) for oral cancer associated with this condition (13).

The popularity of areca-nut containing preparations such as *pan masala* (see paper by Bhonsle *et al.*, this volume) has increased tremendously within the last few years owing to a very sophisticated marketing campaign. In view of the serious consequences of submucous fibrosis and the etiological role of areca-nut chewing, a strict curb on the advertisement and use of these products is warranted.

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# Smoking and chewing habits in Sri Lanka: implications for oral cancer and precancer

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The commonest forms of tobacco use in Sri Lanka are smoking of cigarettes and *beedis* and chewing of betel quid with tobacco. Smoking is almost exclusively practised by men, while the most common habit among women is chewing betel quid with tobacco. Local brands of cigarettes contain more toxic substances than their western counterparts. Cigarette smoking is more popular than *beedi* smoking, and the trends indicate that it is increasing; betel-quid chewing does not appear to be increasing. A case-control study of oral cancer and precancer conducted in Sri Lanka demonstrated high relative risks associated with these habits. The findings suggest a strong need to initiate control measures on tobacco consumption and to reduce the toxicity of various tobacco products.

## INTRODUCTION

Oral cancer is one of the 10 most common cancers in the world (1), and in many South Asian countries it is the commonest cancer (2,3). Over 90% of oral cancers in the Indian subcontinent are attributable to prolonged exposure to local forms of tobacco chewing and smoking (4). This implies that oral cancer is a self-induced disease, which is amenable to primary prevention.

A study on trends in the relative frequency of oral cancer in cancer hospital admissions in Sri Lanka showed a decline in the frequency of oral cancer from 38.5% in 1975 to 29.8% in 1984 (5). This decline may be due partly to recent improvements in the diagnosis of cancers in relatively non-accessible sites.

This paper reviews data on smoking and chewing habits prevalent in the rural population of Sri Lanka on the basis of recent studies, including the National Cancer Control Programme (6), and provides an assessment of the risk from these habits for oral precancer.

## TOBACCO PRODUCTS AND CONSUMPTION

Table 1 gives information on tobacco cultivation and sales in Sri Lanka. The acreage under tobacco increased up to 1983, but since then there has been a 25% drop. The sales trends over the last two decades, however, suggest that tobacco consumption is increasing.

In Sri Lanka, tobacco is used for smoking as cigarettes, *beedis* (syn. *bidis*), cigars and (rarely) in pipes. The tar and nicotine levels in most local brands of cigarettes in Sri Lanka are high by international standards; for example, in five brands investigated in 1982, the tar content ranged from 18.2-24.0 mg and nicotine from 0.8-1.07 mg per cigarette (7), and since then these levels have not changed (8). These concentrations are comparable to the average tar yields in cigarettes in the USA in the 1960s, although there the level has been curtailed drastically to the present average tar level of 13.2 mg (9).

*Beedis* are made by rolling sun-dried coarse tobacco in a wrapper leaf (*Diospyros*



Table 1

*Tobacco production in Sri Lanka, 1972-80<sup>a</sup>*

Year	Area ( $\times 10^3$ acres)	Leaf (CWT)	Cigarettes (millions)	Beedis (millions)	Revenue (million Rs.) <sup>b</sup>
1972	32	809	3424	—	392
1974	24	658	3912	—	373
1976	32	743	4181	—	451
1978	33	708	5098	2036	759
1980 <sup>c</sup>	38	866	5225	1363	1000

<sup>a</sup>Source: ref. (7)

CWT, hundredweight (lbs)

<sup>b</sup>One US\$ = Sri Lankan Rs. 37.50

—, not available

<sup>c</sup>Since 1983, a drop of 25% in the acreage under tobacco cultivation has been noted

*melanoxydon*) into a conical shape and securing the narrow end with a thread. The amount of tobacco in a *beedi* varies from 0.2-0.3 g, in contrast to 1 g of tobacco in a standard-sized cigarette. *Beedis* are mostly made in small-scale industries.

## SMOKING PATTERNS

Smoking patterns in Sri Lanka were recorded in a national study conducted in 1988 (6), and these are reproduced in Tables 2 and 3. In a target population of over 9000 individuals over

the age of 12 years, 54.8% of men and less than 1% of women were smokers. These numbers are comparable to the smoking prevalences in Henan province in China, where 56% of men and 1% of women were smokers, and in rural Bangladesh, where 67% of men and 1% of women were smokers (10). In an earlier study in a limited area in Sri Lanka, 48% of men were reported to be smokers (11), indicating that there may be a slight increase in smoking among men. This finding is in contrast to the decline in consumption in many western countries (12). For example, in the USA, cigarette smoking rates among adult males declined from 40% in 1965 to 29% in 1987 (13).

Specific patterns of smoking in Sri Lanka (Table 3) include cigarette smoking (74%), singly or in combination with other smoking habits (6). This is at variance with the findings in India, where *beedi* smokers outnumber cigarette smokers by about six times (14). Perhaps a changeover from *beedi* smoking to cigarette smoking can be postulated on the basis of the observation of a decline in the production of *beedis* and an increase in cigarette production in Sri Lanka. It was also observed that 7.2% of men were ex-smokers, of whom over half were above the age of 45 years. This is different from the situation in the USA, where nearly half of

Table 2

*Prevalence of smoking in Sri Lanka<sup>a</sup>*

Age group (years)	Males			Females		
	Surveyed (no.)	Smokers		Surveyed (no.)	Smokers	
		No.	%		No.	%
12-20	1181	195	16.5	986	4	0.4
21-40	2786	1834	65.9	1896	15	0.79
41-60	1252	851	67.9	684	10	1.46
≥61	415	206	49.6	140	2	1.43
Total	5634	3086	54.8	3706	31	0.84

<sup>a</sup>Source: ref. (6)



all living adults who ever smoked have quit the habit (13).

**Table 3**

*Distribution of smokers according to specific forms of smoking<sup>a</sup>*

Smoking habit	Males		Females		Both	
	No.	%	No.	%	No.	%
Cigarettes only	1182	37.7	12	36.4	1194	37.7
Cigarettes and beedi	1003	32.0	5	18.2	1008	31.9
Beedi only	466	14.9	7	24.2	473	15.0
Cigars only	239	7.6	3	9.1	242	7.6
Cigarettes and cigars	129	4.1	1	3.0	130	4.1
Cigars and beedi	102	3.3	3	9.1	105	3.3
Cigarettes and pipe	7	0.2	—	—	7	0.2
Pipe and cigars	3	0.1	—	—	3	0.1
Pipe only	1	<0.5	—	—	1	<0.5
Pipe and beedi	1	<0.5	—	—	1	<0.5
Total	3133	100	31	100	3164	100

<sup>a</sup>Source: ref. (6)

—, trivial

## SMOKELESS TOBACCO USE (TOBACCO CHEWING)

Smokeless tobacco used in Sri Lanka is made from sun-dried, coarsely cut tobacco leaves; it is sold loose, complete with the stem, and is consumed raw. Tobacco is chewed by itself by a small proportion of people, but more often it is chewed in a betel quid. Betel-quid chewing in Sri Lanka closely resembles that practised in India (see paper by Bhonsle *et al.*, this volume). As in India, the basic ingredients include betel leaf (*Piper betle*), slaked lime

[Ca(OH)<sub>2</sub>], areca nut (*Areca catechu*) and coarse-leaf tobacco (15). An average chewer consumes 3-10 g of tobacco per day. The ingredients and the method of betel-quid chewing seem to vary with people, ecology, tradition and personal taste.

Table 4 shows the prevalence rates of betel-quid chewing according to age among 1133 villagers. Some 54% of men and 42% of women chewed betel quid. Unlike in India, where most betel-quid chewers include tobacco, only 46% of the men and 63% of the women in the present study included tobacco. Tobacco was chewed alone by 2.6%. Some 5.2% of men and 2% of women were ex-chewers; most of these were over the age of 60 and may have abandoned the habit because elderly people who are edentulous find betel quid difficult to chew.

**Table 4**

*Betel-quid chewing: percentage of regular chewers by age<sup>a</sup>*

Age group (years)	Men (n = 316)	Women (n = 817)
20-29	28	20
30-39	50	32
40-49	68	59
50-59	63	68
60-69	86	79
≥70	75	59
Total	54	42

<sup>a</sup>Source: Warnakulasuriya (1982) (unpublished data)

## EPIDEMIOLOGICAL STUDIES ON CARCINOGENICITY

The causal relationship between tobacco smoking and chewing tobacco, alone or in betel quid, and oral cancer is well documented (16-22). An epidemiological assessment of the carcinogenicity of chewing betel quid with and without tobacco showed that the relative risks



for chewing betel quid without tobacco were either insignificant or were markedly lower than those associated with chewing betel quid with tobacco (23).

Cross-sectional studies on oral precancerous lesions and conditions were reported from Lucknow (24) and Ahmedabad (25) in India and from Malaysia (26). Gupta (27) demonstrated a dose-response relationship between tobacco habits and leukoplakia, which was stronger for smoking than for chewing.

### A CASE-CONTROL STUDY ON ORAL PRECANCER IN SRI LANKA

A community-based case-control study was conducted on oral precancerous lesions and conditions among cases detected in a screening programme in Sri Lanka (28). The cases comprised 359 patients (316 men and 43 women) aged over 20 in whom the lesions were diagnosed by the standard criteria (29,30). An equal number of age- and sex-matched controls from the same villages were examined, and information on tobacco habits was recorded for both cases and controls. Table 5 shows the relative risks for smoking and for

chewing betel quid with and without tobacco. The lowest relative risks, 5.3 among men and 5 among women, were observed among chewers of betel quid without tobacco and were not significant. When the quid was chewed with tobacco, the relative risk was 15.5 ( $p \leq 0.005$ ) for men and 33.0 ( $p \leq 0.001$ ) for women.

### DISCUSSION

In our study, men who chewed betel quid with tobacco carried a higher risk than smokers. This finding is in contrast to that of an Indian study, in which higher relative risks for leukoplakia were observed among smokers than chewers (27). The highest relative risk of 24.7 was seen among men who both smoked and chewed, indicating a synergistic action. It is interesting that our findings are similar to those in other studies on oral cancer from India (18), Sri Lanka (19) and Pakistan (21).

Our findings indicate that tobacco use is fairly extensive in Sri Lanka and also confirms that its use is deleterious to oral health. The increase in cigarette consumption among men and the continued popularity of betel-quid chewing by both genders are of great concern.

Table 5

*Relative and attributable risks for smoking (S) and betel-quid chewing (Q) without and with tobacco (T)*

	No habit	Q	S	QT	S + Q	S + QT
<b>Males</b>						
Precancer	1	5	48	22	115	125
Controls	17	16	84	25	88	86
RR	1	5.3	9.7	15.0	22.2	24.7
$\chi^2$		2.5*	6.9**	9.7***	17.1****	19.3****
AR		70%	88%	91%	95%	96%
<b>Females</b>						
Precancer	1	15	0	26	0	1
Controls	9	27	0	5	0	0
RR	1	5		33		
$\chi^2$		2.5*		15.5****		

\*Nonsignificant; \*\* $p < 0.01$ ; \*\*\* $p < 0.005$ ; \*\*\*\* $p < 0.001$ ; Males,  $n = 316$ ; females,  $n = 43$  in each group



Confounding this problem is the fact that locally made cigarettes deliver far more toxic substances to the users than their western counterparts. This situation warrants the implementation of control measures in the form of primary prevention and reduction in the toxicity of cigarettes as well as other products.

In conclusion, the manufacturing methods for cigarettes and *beedis* in Sri Lanka must be improved to reduce the tar and nicotine

levels in cigarette to at least 15 mg and 1 mg, respectively; proportional reductions are needed for *beedi*. Efforts must be made to make chewing tobacco less hazardous. Intervention methods aimed at preventing people from starting smoking must be adopted to check the rising trend in cigarette smoking in the population. Likewise, appropriate measures must be undertaken to educate people not to start betel-quid chewing or, if not give up, reduce its use substantially; or to begin with, at least exclude tobacco from the betel quid.

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**CONSEQUENCES FOR CANCER  
IN GENERAL**





# The world tobacco-related cancer burden: the weight of the evidence and the need for further research

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An accurate assessment of the tobacco-related cancer burden in the world requires data on (i) mortality or preferably morbidity, (ii) prevalence of tobacco use in its various forms and (iii) the precise relationship between tobacco use and disease for each country. The availability of such data varies considerably from one country to another. Using a variety of approaches, it was estimated that there were about 6.35 million incident cases of the most frequent cancers in 1980. Of these, 49% occurred in the developed and 51% in the developing countries. It is estimated that 1-1.5 million cancers per year are induced by tobacco use.

## INTRODUCTION

The title of this paper, 'The world tobacco-related cancer burden', is somewhat impressive and may appear presumptuous. It was, therefore, necessary to add a subtitle: 'The weight of the evidence and the need for further research', which indicates more appropriately that, although some knowledge is presently available regarding the world tobacco-related cancer burden, quite a lot more needs to become better known. In order to evaluate this burden correctly, one needs to have precise statistics concerning three items: (i) cancer occurrence (mortality or preferably incidence); (ii) prevalence of tobacco use in its various forms, and not only manufactured cigarettes; and (iii) last but not least, the precise relationship between tobacco use and disease for each country.

## CANCER OCCURRENCE

The availability of such data varies greatly from one country to another. An estimation of the availability (as of 1980) of data on cancer

mortality and cancer incidence by United Nations' areas has been produced (1) and is illustrated in Table 1. Although in some countries mortality statistics have been available for over 100 years, the data of the *World Health Statistics Annual* goes back only to 1950-55. For so-called developed countries (Europe, North America, Japan, Australia and New Zealand), the coverage for cancer mortality is close to 100%; for less-developed countries, the coverage is much lower: 16%. It is particularly low in Asia (excluding Japan) and Africa, where cancer mortality statistics by specific cancers are available for only a very small proportion of the population. The situation is, of course, even worse for incidence. Whereas it was estimated that mortality data were available for 37.5% of the world population, for incidence the proportion is only 14%, corresponding to 58% for developed countries and only 2.3% for less developed ones. An additional difficulty is that the populations covered by cancer registries are often not representative of the countries as a whole (1). In some countries, registries do not exist in large cities with multiple



**Table 1***Availability (as of 1980) of data on mortality from and incidence of cancer for selected United Nations' areas<sup>a</sup>*

Area	Population (millions)	% of population for which data are available	
		Mortality	Incidence
World	4453	37.5	14
Developed countries	1136	100	58
Less developed countries	3317	16	2.3
Africa	476	9	0.5
Latin America	362	97	9.6
North America	252	100	34
Asia	2591	10	3.3
China	1003	0	1
Japan	117	100	43
Other eastern Asia	63	8	8
Southeastern Asia	362	27	2.4
Southern Asia	949	1.5	1
Western Asia	98	14	53
Europe	484	99	26
Oceania	23	81	81
USSR	265	100 <sup>b</sup>	100 <sup>b</sup>

<sup>a</sup>Source: ref. (1)<sup>b</sup>Some sites only

sources of medical care, and, therefore, the registries tend to include only a rather rural population; in other countries, the opposite is true, with major cities being over-represented. Bombay, for example, has a registry dating back to 1963 and covering a very large population of about nine million people for Greater Bombay (2).

In the absence of an exhaustive coverage of data on cancer incidence, some attempts at estimation have nevertheless been made. One of the first was carried out in 1984 by Parkin *et al.* who estimated data for the year 1975 (3), and a subsequent update to 1980 published in 1988 (4). The methods of estimation rely on incidence data from population-based cancer registries, when they exist. When no incidence data were available, cancer incidence was estimated from cancer mortality data, using conversion factors obtained from 20 countries where both incidence and mortality are

known. When mortality by cause was not sufficiently reliable, cause-specific mortality rates were derived from crude death rates and age-specific death rates for broad causes of death from populations at various stages of development. The estimated incidence rates for the 16 less developed regions are shown in Table 2. India has an incidence rate for all cancers (excluding skin) of around 100 new cases per 100 000 person-years, for both males and females.

From the rates for all sites, using data from cancer registries providing estimates of the proportionate distribution of cancers within the total, cancer incidence rates specific for 16 common sites were calculated. As an example, the estimated crude rates of lung cancer incidence are shown in Table 3. Rates vary from 1.0 in western Africa to 98.1 per 100 000 in northern Europe for men, and from 0.4 in eastern Africa to 30.3 in northern America for



**Table 2**

*Estimated incidence rates of cancer of all sites (excluding skin) for selected United Nations' areas<sup>a</sup>*

Area	Male (per 100 000 person-years)	Female
Eastern Africa	78	97
Middle Africa	80	106
Northern Africa	97	105
Southern Africa	117	122
Western Africa	72	90
Caribbean	129	112
Central America	48	66
Temperate South America	245	214
Tropical South America	73	77
China	141	114
Other eastern Asia	113	131
Southeastern south Asia	69	94
Southern Asia	94	95
Western Asia	104	108
Melanesia	99	100
Micronesia	73	87

<sup>a</sup>Source: ref. (4)

women (4). The world variability in lung cancer occurrence is quite large. If lung cancer occurrence is expressed as the percentage of all cancers for people of each sex combined, it represents less than 5% of all cases in most of Africa, 5-10% in Asia and southern America, 10-15% in Australia and parts of Europe, and more than 15% in northern America, the USSR and northern Europe. Asia is among the low-percentage countries, although in Africa the percentage is even lower.

The most frequent cancers in the world are presented in Table 4. The total number of all incident cases in 1980 was estimated at about 6.35 million — 3.25 in men and 3.10 in women (4). For men, lung cancer comes first, with 514 000 new cases or approximately 16% of all new cancer cases. It is followed by cancers of the stomach, colon and rectum, mouth and pharynx, prostate and oesophagus. For females, breast cancer comes first, followed by cervical, colo-rectal, gastric and corpus uterine

cancers, with lung in fifth position. If the two sexes are combined, in 1980 stomach cancer was in first position followed by lung, but given the decrease observed for the former and the increase in the latter, the situation is now reversed and lung cancer comes first. More recent estimates are that 2.0-2.7 million deaths per year (5,6) are attributable to tobacco-related diseases, including, but not limited to, cancer; and this figure could increase to approximately 8.0 million by the year 2025.

Of the 6.35 million new cancer cases, 49.3% occurred in the developed countries and 50.7% in the developing countries; whereas, the population ratio is 1:3. Although cancer is

**Table 3**

*Estimated crude rates of lung cancer incidence by United Nations' areas<sup>a</sup>*

Area	Male (per 100 000 person-years)	Female
Eastern Africa	1.8	0.4
Middle Africa	3.2	1.3
Northern Africa	4.0	0.7
Southern Africa	14.8	4.1
Western Africa	1.0	0.3
Caribbean	28.4	9.5
Central America	6.6	3.2
Temperate South America	35.6	6.4
Tropical South America	17.5	4.9
Northern America	74.6	30.3
China	8.5	4.7
Japan	31.0	11.2
Other east Asia	22.0	5.9
Southeastern south Asia	12.4	3.9
Southern Asia	7.3	1.5
Western Asia	13.0	3.3
Eastern Europe	61.2	10.1
Northern Europe	98.1	29.5
Southern Europe	64.2	8.9
Western Europe	86.7	12.3
Australia/New Zealand	61.6	15.9
Melanesia	3.3	1.0
Micro-/Polynesia	22.6	6.5
USSR	51.2	10.3

<sup>a</sup>Source: ref. (4)



**Table 4**  
*The most frequent cancers in the world<sup>a</sup>*

Both sexes			Males			Females		
Site	Thousands	%	Site	Thousands	%	Site	Thousands	%
Stomach	669.4	10.5	Lung	513.6	15.8	Breast	572.1	18.4
Lung	660.5	10.4	Stomach	408.8	12.6	Cervix	465.6	15.0
Breast	572.1	9.0	Colon/Rectum	286.2	8.8	Colon/Rectum	285.9	9.2
Colon/Rectum	572.1	9.0	Mouth/pharynx	257.3	7.9	Stomach	260.6	8.4
Cervix	465.6	7.3	Prostate	235.8	7.3	Corpus uteri	148.8	4.8
Mouth/pharynx	378.5	6.0	Oesophagus	202.1	6.2	Lung	146.9	4.7
Oesophagus	310.4	4.9	Liver	171.7	5.3	Ovary	137.6	4.4
Liver	251.2	4.0	Bladder	167.7	5.2	Mouth/pharynx	121.2	3.9
Lymphoma	237.9	3.7	Lymphoma	139.9	4.3	Oesophagus	108.2	3.5
Prostate	235.8	3.7	Leukaemia	106.9	3.3	Lymphoma	98.0	3.2

<sup>a</sup>Source: ref. (4)

already important for both developed countries and developing countries, the patterns are different. Cancers of the lung, breast and colorectum are found predominantly in developed countries; whereas, cervical, buccal and pharyngeal, oesophageal and hepatic cancers are more frequent in the developing countries. The ranking of the different cancers varies from region to region. For northern America, lung cancer comes first in men and third in women; in the USSR and Europe, lung cancer comes first among men but does not yet rank among the first five cancer sites in women. Among the developed countries, Japan is an exception by the importance of gastric cancer, which comes first in both men and women and weighs very strongly in the almost equal division of stomach cancer among developed and developing countries. The situation is quite different in other parts of the world. In China, lung cancer ranks fourth among men; whereas, it is first in the southeast region of southern Asia — almost equal in importance to cancer of the mouth and pharynx. It does not yet come into the picture in western Africa. In southern Asia, buccal and pharyngeal cancer comes first in men and third in women, lung cancer being second for males (4).

## TOBACCO-RELATED CANCERS

What do the above figures tell us about tobacco-related cancers? The predominance of lung cancer is undoubtedly linked to tobacco use. It has been repeatedly suggested that lung cancer can be used as a reliable marker of exposure to tobacco, taking into account latency, cohort effects and 'maturity' of tobacco exposure. On a world scale, lung cancer represents, for the two sexes combined, between 1% and 2% of all cancers in western Africa to 17.9% in northern Europe, with a global estimate of 10.4%. Yet, lung cancer is not the only cancer linked to tobacco use, and in countries like India, it would be a misleading indicator of use. In fact, according to *Cancer Incidence in Five Continents* (7), it is in India that the highest rate (15.2 per 100 000) of oral cancer occurs (among women in Bangalore) and the lowest male lung cancer incidence rate (5.8 per 100 000 among men in Madras). In this country, therefore, cancer of the buccal cavity can be used as an indicator of tobacco use instead. Although the correlation between the number of manufactured cigarettes and lung cancer rates in middle-age works very well, as shown by Doll and Peto (8), we should therefore also consider cancers at other sites.



According to the *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans* (Volume 38), "there is 'sufficient' evidence that tobacco smoke is carcinogenic to humans (as well as to experimental animals). The occurrence of malignant tumours of the respiratory tract and of the upper digestive tract is causally related to the smoking of different forms of tobacco (cigarettes, cigars, pipes, and *bidis*). The occurrence of malignant tumours of the bladder, renal pelvis, and pancreas is causally related to the smoking of cigarettes" (9). A companion and preceding monograph to the one on tobacco smoking was the *IARC Monographs* (Volume 37) on *Tobacco Habits other than Smoking; Betel-quid and Areca-nut Chewing, and Some Related Nitrosamines* (10). Overall, it was considered that "there is 'sufficient' evidence that the oral use of snuffs of the types commonly used in North America and western Europe are carcinogenic to humans. There is 'limited' evidence that chewing tobacco of the types commonly used in these areas is carcinogenic. Epidemiological studies that did not distinguish between chewing tobacco and snuff provide 'sufficient' evidence for the carcinogenicity of oral use of smokeless tobacco products as reported in these studies. In aggregate, there is 'sufficient' evidence that oral use of smokeless tobacco of the above types is carcinogenic to humans. There is 'sufficient' evidence that oral use of tobacco mixed with lime is carcinogenic to humans. There is 'inadequate' evidence that oral use of the other smokeless tobacco preparations considered (*nass*, *naswar*, *mishri*, *gudhaku*, and *shammah*) is carcinogenic to humans. There is 'inadequate' evidence that nasal use of snuff is carcinogenic to humans. There is 'inadequate' evidence to evaluate the carcinogenicity of chewing tobacco, snuff or *nass* to experimental animals" (10). As we can see, the problem of smokeless tobacco products is more complex, less clear, and has been studied less than tobacco smoking, in particular for rather uncommon cancer sites. For betel quid, the

IARC Monographs (Volume 37) concludes: "There is 'sufficient' evidence that the habit of chewing betel quid containing tobacco is carcinogenic to humans. There is 'inadequate' evidence that the habit of chewing betel quid without tobacco is carcinogenic to humans. The Working Group also concluded that, while there is 'sufficient' evidence that the combined habits of smoking tobacco and chewing betel quid without tobacco cause oral and pharyngeal cancer, the evidence considered here does not allow an assessment of the possible contribution of betel quid without tobacco to this carcinogenic risk. There is 'limited' evidence that aqueous extracts of betel quid with and without tobacco are carcinogenic to experimental animals. The data are 'inadequate' to allow an evaluation of the carcinogenicity of betel quid or arecoline to experimental animals" (10).

### TRENDS IN TOBACCO USE AND CONSEQUENT CANCER OCCURRENCE

After the above review of the cancer burden and a summary of the scientific evidence incriminating tobacco as a human carcinogen, how can we link the two quantitatively in terms of the proportion of all cancers attributable to smoking? Looking at trends in tobacco use and subsequent cancer occurrence may help in understanding the problem. Examination of the relative changes for men and women, comparing mortality in 1985-86 for developed countries relative to the mortality rate in 1950-54, shows that until recently for men the highest increase in the cause-specific mortality has been for lung cancer; for women, the relative change has been even more striking and the increase continues (11). Increases in the incidence of lung cancer in the USA, the United Kingdom and most other western countries have been closely linked to the use of manufactured cigarettes (12). But in the United Kingdom and the USA, the trends are now starting to change, and a decrease



has been observed, at least in some birth cohorts (8). Therefore, after some impressive increases, at last a change is taking place.

Given the fact that the rest of the world began cigarette smoking with some delay compared to the United Kingdom and the USA, we here are at a different phase of development. Looking at the change in the overall use of manufactured cigarettes in six geographical areas between 1970 and 1985, we see that the increase is greatest in Africa and quite marked in Asia. In contrast, a decrease is seen in the USA and Canada and in Oceania/Australasia (13). In the world as a whole, there has been an increase in cigarette use due to the large increases in Africa, Latin America and Asia, which have more than compensated for the decreases in the United Kingdom and the USA (14). It is still too early to see the full impact on lung cancer in places like Bombay where cigarette smoking is not the only form of tobacco consumption, but the effects are already apparent in Singapore (15). Changes in the incidence of lung cancer have been responsible for a large part of the reported increase in mortality from all cancers. WHO estimates that 76% of the overall change in men is due to an increase in the incidence of lung cancer, after adjustment for age and size of population (16). Although at present 'only' 31% of lung cancer cases occur in the developing countries, this proportion will probably increase (14). Indeed, the situation is very worrying, with the proportion of smokers in the male population at about 50% or more in a number of developing countries. This situation is not specific to developing countries and still exists in parts of Europe (14).

**Future cancer occurrence:** Exactly how many more cancer cases can we expect in the future? Forecasts need to take into account demographic factors (size and age structures of the population) as well as changes in, either cross-sectional or cohort-specific risks. Some investigators object that these can only be

informed guesses, whereas others try to build up comprehensive models. Such an exercise is currently being conducted at WHO, Geneva, in order to estimate better the proportion of smoking-attributable mortality for the world as a whole (6). The need for such an exercise stems from the present lack of reliable data. Good estimates exist for the USA, based mainly on 'cancer prevention studies', and these were reported in the 1989 *US Surgeon-General's Report* (12). In 1985, 90% of lung cancer was attributable to smoking for men and 79% for women. Figures have also been presented for Japan (17). But how applicable are these estimates for the rest of the world? My modest answer is that at present we do not know exactly, the main reason being that, for example, lung cancer in females appears to behave differently in some parts of the world, as in China where nonsmoking women tend to have high rates, mainly of adenocarcinoma (7). We need to study this problem better in parts of the world where little is known at present, such as Africa, and future calculations should take into account the importance of tobacco products other than cigarettes, as the Indian experience demonstrates. This is also of the utmost importance for diseases other than cancer which are linked to smoking, in particular cardiovascular diseases, chronic obstructive lung disease and tuberculosis. A lot of work remains to be done.

## CONCLUSION

To conclude on a humorous note, we, as doctors, have sometimes acted (and have been used) as poor role models. As members of the so-called developed countries, we should stop being poor role models for the rest of the world. We must have better things to export than tobacco.

And now a word of hope. Based on comparisons between highest and lowest observed cancer incidence in various populations of the world, it is estimated that potential or substantial reductions in incidence can be achieved



Table 5

*Theoretical possible reductions in the incidence of cancer due to elimination of smoking<sup>a</sup>*

Site	Measures to be taken	Areas	Possible reduction (%)
Oral cavity	Elimination of tobacco chewing and smoking	Asia, Europe	60-80
Oesophagus	Elimination of tobacco and reduction of alcohol	USA, southern Europe, India	75 35
Pancreas	Elimination of smoking	World	30
Lung	Elimination of smoking	World	80-90 (Men) 60-80 (Women)
Larynx	Elimination of smoking and reduction of alcohol	World	85
Cervix	Elimination of smoking	'Western' countries	20-25
Bladder	Elimination of smoking	World	30-70
Kidney	Elimination of smoking	'Western' countries	30-40

<sup>a</sup>Source: ref. (4)

by the elimination of tobacco (1). Table 5 presents the main targets. Applying these estimates to the 1980 data presented at the beginning of this paper, we end up with an estimate of about 1.0-1.5 million cancers per year that

are induced by tobacco use. Adding in the other diseases linked to tobacco, this figure represents at least two million deaths per year for the entire world population, which are truly avoidable.

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# Lung cancer and other diseases related to passive smoking: a large-scale cohort study

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In 1981, we demonstrated an elevated risk of lung cancer among nonsmoking wives of husbands who smoke; subsequently, there have been several studies on this topic. Seventeen out of the 22 studies published in 1989 showed elevated risks; in seven studies, the risks were statistically significant. The risks in 10 selected studies were mostly higher when husbands smoked more heavily, the average relative risks for lung cancer in nonsmoking women with nonsmoking husbands, light smoking husbands and heavy smoking husbands being 1.00, 1.41 and 2.38, respectively. In addition to lung cancer, our cohort study revealed significantly elevated risks for nasal sinus cancer, brain tumour, post-menopausal breast cancer and ischaemic heart disease in nonsmoking women with heavily smoking husbands as compared to those with nonsmoking husbands. These effects are due to carcinogens and other toxic substances, which are present in higher concentration in sidestream smoke than in mainstream smoke.

## INTRODUCTION

Since our report on the effect of husbands' smoking on the lung cancer risk in nonsmoking wives (1), many studies have been conducted to examine the passive smoking-lung cancer hypothesis. The results of most of these studies were in line with our report, as reviewed by the US Surgeon-General (2) and others (3-7).

The purpose of this paper is to summarize the results of our study in Japan, with special reference to lung cancer and other selected causes of death the risk of which is elevated by passive smoking.

## MATERIAL AND METHODS

In our large-scale cohort study in Japan, 9106 deaths were recorded among 91 450 nonsmoking wives whose husbands' smoking habits were known during the 16-year follow-up

(1966-81). The risk of nonsmoking wives dying from lung cancer (n=200), ischaemic heart disease (n=494) and other selected causes of death was measured according to the extent of the husbands' smoking habit.

## RESULTS

The results are summarized in Tables 1-4. Those diseases that showed a significant elevation in risk in nonsmoking wives with husbands who smoked 20 or more cigarettes daily are listed in Tables 1 and 2; associations with the extent of husbands' smoking (dose-response relationships) are shown in Tables 3 and 4.

**Lung cancer:** Out of 429 female lung cancer deaths that took place during the 16-year follow-up period, 303 were in nonsmokers. Of these women, 200 were from 91 450

Table 1

Relative risks<sup>a</sup> of cancer of selected sites for nonsmoking wives with heavily smoking husbands (20 or more cigarettes daily). Risk for wives with nonsmoking husbands = 1.00. Cohort study, 1966-81, Japan

Site of cancer	n	Relative risk	90% Confidence limits	One-tailed <i>p</i>
Brain tumour	34	4.78	1.62 - 14.11	0.008
Nasal sinus	28	3.29	1.36 - 7.96	0.013
Leukaemia	51	2.04	1.09 - 3.82	0.030
Lung	200	1.90	1.94 - 2.70	0.001
Breast	115	1.73	1.12 - 2.66	0.018
Malig. lymphoma	85	1.58	0.89 - 2.81	0.096
Liver	226	1.31	0.94 - 1.82	0.094
Bone	17	1.31	0.33 - 5.21	0.373
Cervix	273	1.28	0.95 - 1.74	0.089
Bile duct/Gallbladder	91	1.25	0.79 - 1.98	0.215
All sites	2705	1.21	1.10 - 1.32	0.000
Colon	142	1.11	0.77 - 1.61	0.318
Ovary	54	1.08	0.54 - 2.15	0.428
Urinary organs	49	1.03	0.50 - 1.91	0.468
Upper digestive tract	80	1.01	0.58 - 1.78	0.486
Rectum	112	1.01	0.64 - 1.60	0.484
Stomach	854	1.01	0.86 - 1.19	0.463
Pancreas	127	0.87	0.56 - 1.34	0.295

<sup>a</sup>Adjusted for husband's age by the Mantel-Haenzel method

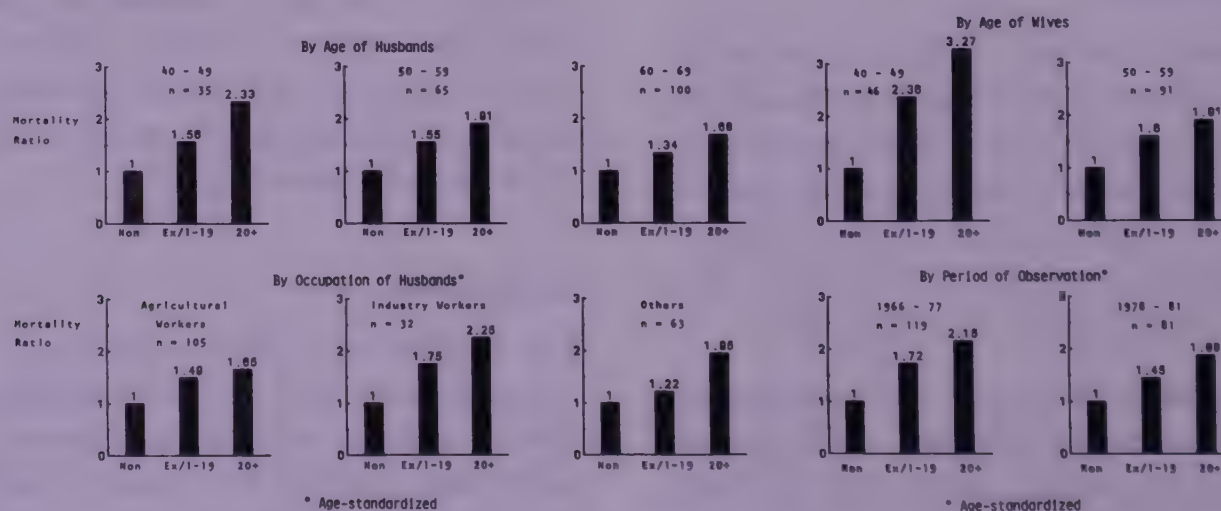


Fig. 1. Mortality ratios for lung cancer in nonsmoking wives by husband's smoking habit (prospective study, 1966-81, Japan)

nonsmoking wives whose husbands' smoking habits were known. The extent of the elevation in risk for lung cancer in nonsmoking wives was studied in relation to the smoking habits of the husbands.

The standardized mortality ratios for lung cancer in nonsmoking women were 1.00, 1.36, 1.42, 1.58 and 1.90 when their husbands were nonsmokers, ex-smokers, daily smokers of 10-14, 15-19 and 20 or more cigarettes per day,



**Table 2**

*Relative risks<sup>a</sup> of selected causes of death for nonsmoking wives with heavily smoking husbands (20 or more cigarettes daily). Risk for wives with nonsmoking husbands = 1.00. Cohort study, 1966-81, Japan*

Cause of death	n	Relative risk	90% Confidence limits	One-tailed <i>p</i>
Stomach ulcer	57	1.73	0.80 - 3.75	0.121
Subarachnoid haemorrhage	126	1.69	1.08 - 2.65	0.026
Emphysema	106	1.49	0.92 - 2.39	0.085
Suicide	200	1.46	1.07 - 1.63	0.019
Hypertensive disease	61	1.46	0.77 - 2.77	0.166
Ischaemic heart disease	494	1.31	1.06 - 1.63	0.019
Hypertensive heart disease	226	1.29	0.93 - 1.78	0.100
Cerebral haemorrhage	1179	1.25	1.08 - 1.43	0.036
Nephritis, nephrosis	128	1.27	0.83 - 1.93	0.399
Gastritis, enteritis	57	1.23	0.70 - 2.16	0.277
Diabetes	227	1.23	0.89 - 1.69	0.147
Cancer	2705	1.21	1.10 - 1.32	0.000
Ill-defined cerebrovascular disease	438	1.20	0.95 - 1.51	0.097
All sites	9106	1.19	1.13 - 1.26	0.000
Other heart disease	680	1.19	0.97 - 1.44	0.073
Pneumonia	258	1.15	0.84 - 1.59	0.232
Tuberculosis	100	1.15	0.71 - 1.86	0.321
Cholelithiasis	30	1.04	0.35 - 3.07	0.476
Arteriosclerosis	68	1.01	0.60 - 2.01	0.399
Cerebral thrombosis	992	1.00	0.85 - 1.17	0.493
Chronic rheumatic heart disease	106	0.86	0.55 - 1.34	0.286
Senility	164	0.81	0.53 - 1.24	0.204
Liver cirrhosis	180	0.75	0.52 - 1.08	0.094

<sup>a</sup>Adjusted for husband's age by the Mantel-Haenzel method

respectively (*p* for trend: 0.00178). A similar, significant dose-response relationship was observed by age and by occupation of husbands, by age of wives, and in each period of observation (Fig. 1), and also when other risk factors such as diet, prefecture and population density were adjusted for (Fig. 2) (8,9).

No other characteristic of the husbands or wives themselves, other than the amount of husbands' smoking, was found to elevate the risk of lung cancer in nonsmoking partners (Fig. 3).

Similar studies have been conducted in many countries. Most were case-control

studies (10-27), and only a few were cohort studies (28,29). The results of most (17 out of 22 reported by 1989) were in line with the results of our study in Japan (Tables 5 and 6) (external consistency).

The earlier the age of marriage to husbands who smoked, higher was the risk for lung cancer in nonsmoking wives, suggesting the importance of duration of exposure to passive smoking (Fig. 4) (30). It was also observed that the risk for lung cancer in nonsmoking husbands was significantly higher when their wives were smokers rather than nonsmokers. Therefore, nonsmokers with a nonsmoking

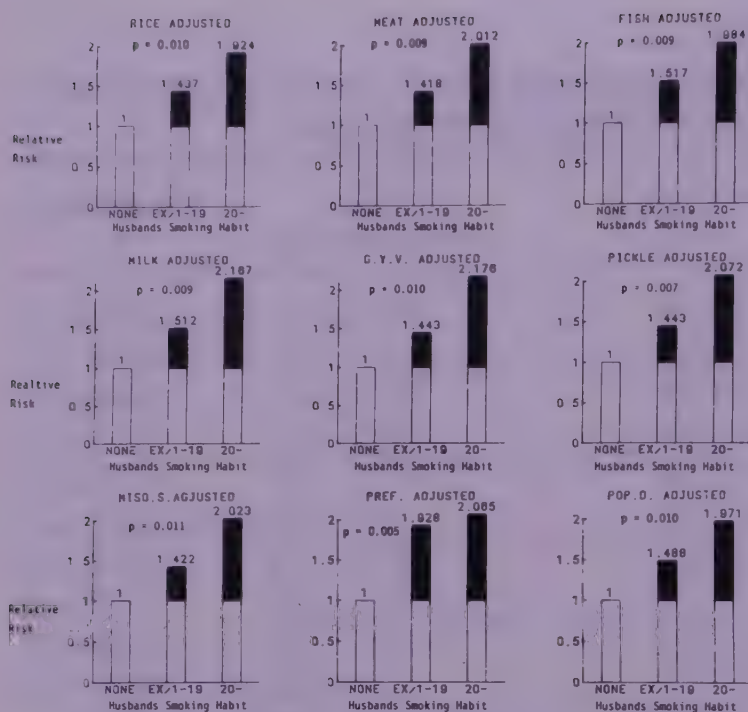


Fig. 2. Relative risk for lung cancer in nonsmoking wives by smoking habit of husbands. Comparison of 200 lung cancer cases and age-occupation matched controls. Observation by selected life style and demographic variables (prospective study, 1966-81, Japan)

spouse should be selected as the unit risk group in order to study the effect of exposure to tobacco smoke on lung cancer, either actively or passively (Fig. 5).

**Other cancers:** For most other sites, no significant association was observed between the risk in nonsmoking wives and the amount of

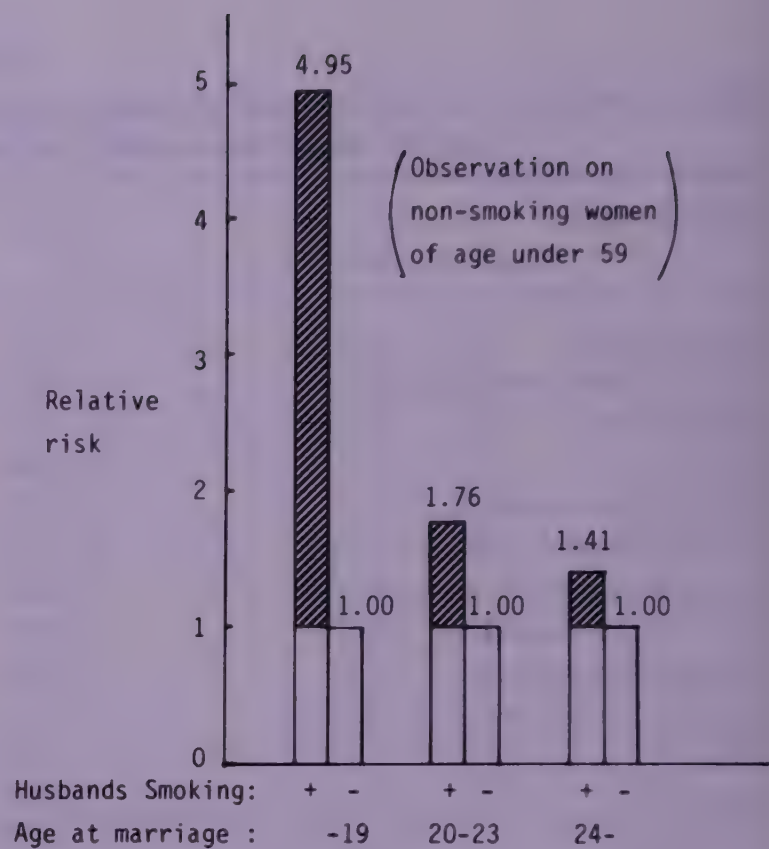
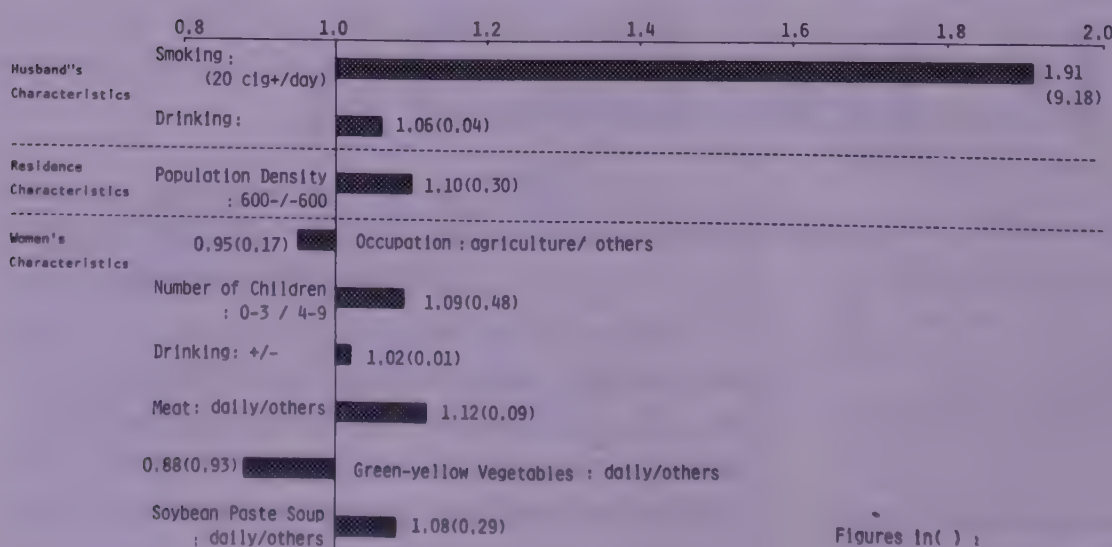


Fig. 4. Lung cancer risk in nonsmoking wives by husbands' smoking habit and by age at marriage (prospective study, 1966-81, Japan)

smoking of husbands. However, a significant elevation of risk for cancers of the paranasal sinuses, breast and brain, and leukaemia in nonsmoking wives was detected, according to the amount of the husband's smoking (Table 3).



Figures in ( ) :  
chi square value

Fig. 3. Lung cancer mortality in nonsmoking women. Ratio by selected risk factors (prospective study, 1966-81, Japan)



The risk for breast cancer, although of borderline significance, when analysed by age groups of wife or standardized by occupation of husbands, revealed a significant dose-response relationship. At age 50-59 years when husbands smoked 1-19 and 20 or more cigarettes daily, the relative risk for mortality from breast cancer was 1.3 and 2.68, respectively ( $p$  for trend: 0.00969) (Fig. 6). The effect was independent of each of the other risk factors for wives, such as number of children (Fig. 7).

**Other causes of death:** Other causes of death in which the risk in nonsmoking wives is significantly associated with the amount of

their husbands' smoking were ischaemic heart disease, subarachnoid haemorrhage, cerebral haemorrhage, suicide and all causes of death (Table 4).

## DISCUSSION

The validity of interview-based information on exposure to passive smoking, on which the current study was based, was clearly demonstrated by recent IARC studies (31) that were conducted in 13 centres in 10 countries by measuring urinary cotinine levels.

For lung cancer, enough evidence to satisfy epidemiological criteria such as consistency

**Table 3**

*Relative risks of cancers at selected sites for nonsmoking wives by husbands' smoking habits; dose-response relationship. Cohort study, 1966-81, Japan*

Site of cancer	Husbands' smoking habit			Mantel-extension chi	One-tailed $p$
	Nonsmoker	1-19 daily	$\geq 20$ daily		
Lung	1.00	1.44	1.90	2.990	0.001
Nasal sinus	1.00 <sup>a</sup>	2.28	3.29	2.064	0.019
Brain	1.00	4.01	4.78	2.069	0.019
Breast	1.00	1.12	1.73	1.795	0.036
Leukaemia	1.00 <sup>a</sup>	1.79	2.04	2.009	0.022
All sites	1.00	1.11	1.21	3.143	0.000

<sup>a</sup>Including ex-smoking husbands

**Table 4**

*Relative risks of selected causes of death for nonsmoking wives by husbands' smoking habits; dose-response relationship. Cohort study, 1966-81, Japan*

Site of cancer	Husbands' smoking habit			Mantel-extension chi	One-tailed $p$
	Nonsmoker	1-19 daily	$\geq 20$ daily		
Cancer	1.00	1.11	1.21	3.143	0.000
Ischaemic heart disease	1.00	1.14	1.31	2.164	0.015
Subarachnoid haemorrhage	1.00	1.52	1.69	1.846	0.032
Cerebral haemorrhage	1.00	1.31	1.25	2.680	0.036
Suicide	1.00	1.34	1.46	2.030	0.021
All causes	1.00	1.15	1.19	5.449	0.000

**Table 5***Relative risks for lung cancer among nonsmoking women, according to number of cigarettes smoked per day by their husbands*

Author(s)	Ref. no.	Husbands' smoking status		
		Nonsmoker	Light	Heavy
Correa <i>et al.</i>	14	1.0	1.2	3.5
Trichopoulos <i>et al.</i>	26	1.0	2.4	3.4
Inoue <i>et al.</i>	19	1.0	1.2	3.4
Pershagen <i>et al.</i>	24	1.0	1.0	3.2
Akiba <i>et al.</i>	10	1.0	1.4	2.1
Wu <i>et al.</i>	27	1.0	1.2	2.0
Garfinkel <i>et al.</i>	16	1.0	1.1	2.0
Hirayama <sup>a</sup>	8	1.0	1.4	1.9
Koo <i>et al.</i>	21	1.0	1.9	1.2
Garfinkel <sup>a</sup>	28	1.0	1.3	1.1

<sup>a</sup>Prospective study; all others are case-control studies.**Table 6***Relative risks (R) for lung cancer in women who had never smoked but had smoking husbands*

Senior author	Ref. no.	Lung cancers	R	Senior author	Ref. no.	Lung cancers	R
Inoue	19	22	2.25	Garfinkel	16	134	1.31*
Geng	17	54	2.16**	Wu	27	<29	1.20
Trichopoulos	26	77	2.11**	Pershagen	24	67	1.20
Correa	14	22	2.07*	Gao	15	226	1.19
Lam	36	60	2.01**	Garfinkel	28	153	1.17
Humble	18	<28	1.80	Shimizu	25	90	1.10
Brownson	11	19	1.68	Gillis	29	8	1.00
Lam	22	199	1.65**	Lee	23	32	1.00
Koo	21	88	1.64	Kabat	20	24	0.79
Hirayama	1,8	183	1.63**	Buffler	12	41	0.78
Avika	10	94	1.50	Chan	13	84	0.75

\*Significant only in trend analysis or in subjects validated as heavy smokers

\*\*Significant at 95% confidence level in comparison of exposed and non-exposed subjects

Modified from ref. (7)

of association, specificity of association and dose-response relationship has already been accumulated in the literature to evaluate the risk of nonsmoking women with smoking husbands.

A different histological pattern of lung cancer in women than in men, e.g., predominance of adenocarcinoma, is considered to be due to the higher proportion of passive smoking-related cases in women than in men.

The results of our large-scale cohort study in Japan further showed an elevated risk

for cancers of the nasal sinus, breast and brain and leukaemia in addition to lung cancer.

An elevation in risk for nasal sinus cancer, as in the case of lung cancer, is compatible with the existence of potent carcinogens in sidestream smoke, which is inhaled through the nose in even higher concentration than in mainstream smoke.

A significant elevation in risk due to passive smoking was reported for childhood brain tumours (32,33); a similar elevation related to



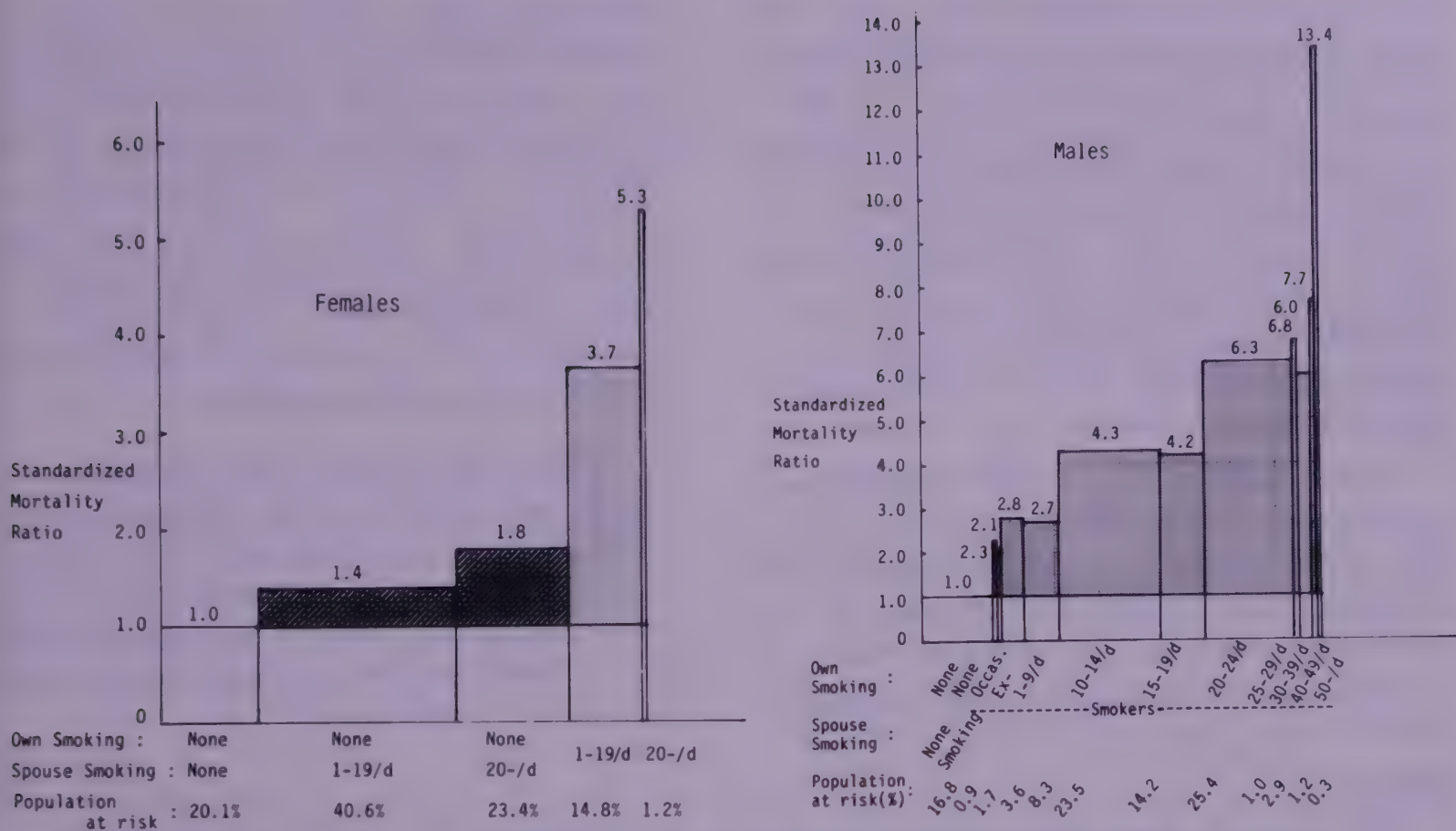


Fig. 5. Active and passive smoking and lung cancer mortality (prospective study, 1966-81, Japan)

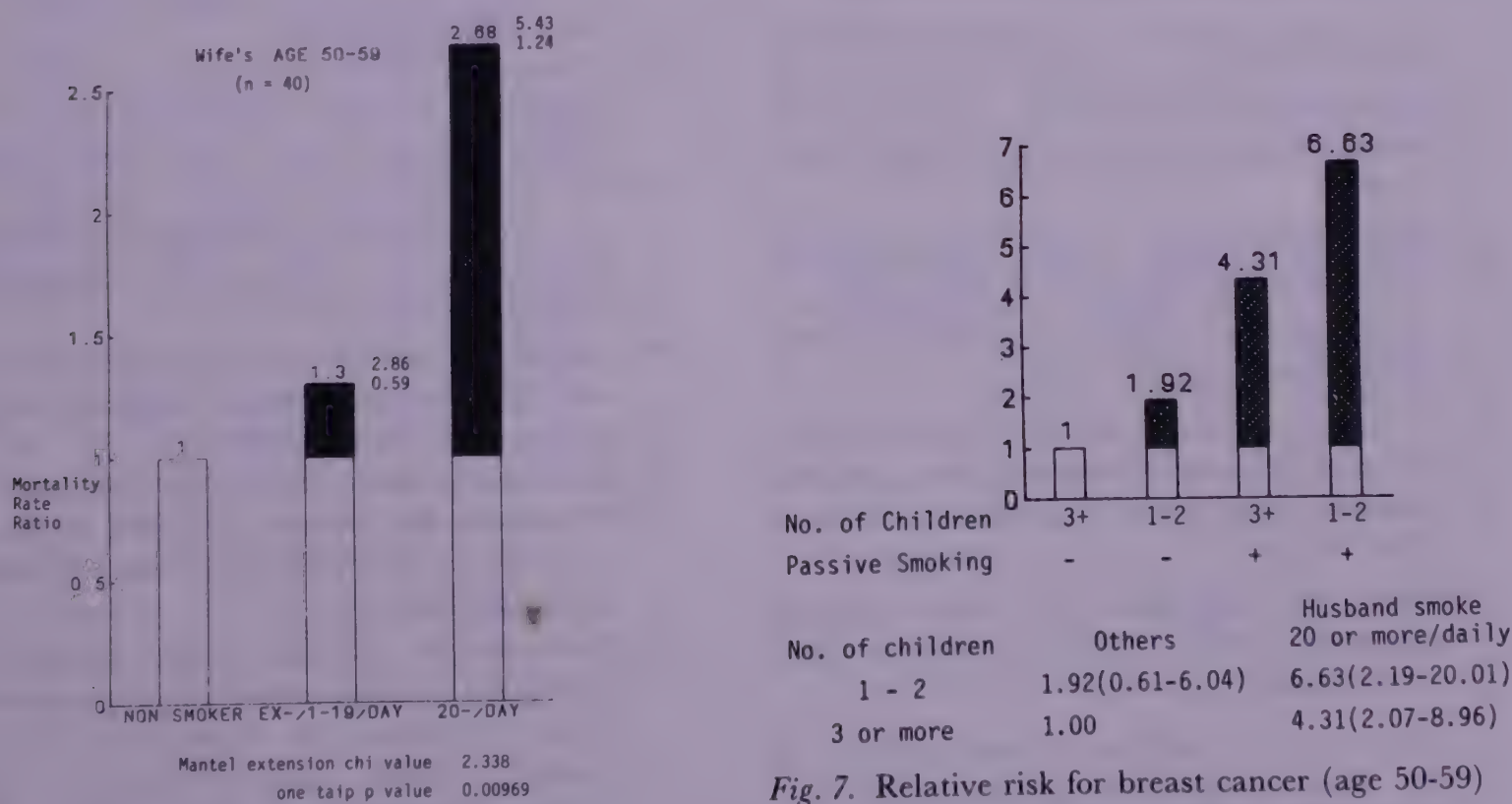


Fig. 6. Rate ratio for death from breast cancer in nonsmoking women by husbands' smoking habit

Fig. 7. Relative risk for breast cancer (age 50-59) in nonsmoking women by number of children and by husbands' smoking habit

passive smoking was also observed for adult brain tumours.

For breast cancer, the observed association is similar to that reported by Sandler *et al.*





# Tobacco-related cancers in Bombay, India: a study of incidence over two decades

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A study of the site-specific incidence rates of cancers of the upper alimentary and respiratory tracts over two decades among males in Bombay showed that the incidence of cancers of the tongue, oropharynx and larynx have decreased significantly, whereas that of oral cancer excluding the tongue has remained more or less stable. The incidences of cancers of the hypopharynx, oesophagus and lung increased only marginally, but successive birth cohorts showed no consistent pattern. Limited data on tobacco habits in Bombay indicate a marked decrease in the proportion of *bidi* smokers in younger cohorts, which conforms with the observed decline in the incidence of those cancers for which *bidi* smoking is the predominant risk factor. For cancers of the hypopharynx, oesophagus and lung, for which tobacco chewing or cigarette smoking is an equally or more important risk factor than *bidi* smoking, no consistent pattern was seen. Tobacco-related cancers constitute about 50% of cancers among men in India. As the recent national trends in *per-caput* consumption of tobacco are different from those in Bombay, the decline in predominantly *bidi* dependent cancers seen in Bombay cannot be extrapolated to the country as a whole. Consequently, control programmes are needed for all smokers in the country, and especially for cigarette smokers in urban areas.

## INTRODUCTION

Tobacco is a major risk factor for cancers of the upper alimentary and respiratory tracts, which constitute about 50% of all cancers among Indian men. This paper examines the trends in the incidence of these cancers over the years.

## TRENDS IN TOBACCO-RELATED CANCERS

Data on site-specific incidence of cancer are available from the Bombay Cancer Registry for a period of over two decades (1,2), making it possible to assess trends in tobacco-related cancers. When the age-adjusted incidence rates for these cancers in five-year periods between 1964-82 (except 1964-66, which is a three-year period) were examined, the incidence of cancer of the tongue declined progressively, from 14 per 100 000 in the early 1960s

to 9.7 per 100 000 in the period 1978-82, while those of cancers of other parts of the mouth remained more or less stable over the years, with an age-adjusted incidence rate of about 7 per 100 000 (Table 1). The rate for cancer of the oropharynx declined from 6.1 per 100 000 to 3.5 per 100 000 over the years, the decline being marked in the late 1970s and early 1980s. The incidence of cancer of the hypopharynx and oesophagus, however, increased from 7.3 to 10.0 per 100 000 and from 13 to 15 per 100 000, respectively. The age-adjusted incidence rate for cancer of the larynx declined from 13.8 to 10.1 per 100 000, whereas that for cancer of the lung increased marginally from 13.3 in the 1960s to 15.8 per 100 000 in the 1980s.

A clearer picture of changing incidence rates was obtained for each site by fitting a



**Table 1***Site-specific age-adjusted incidence rates for cancers at major tobacco-related sites in males in Bombay, 1964-82*

Site of malignant neoplasm	Age-adjusted incidence rate (world) per 100 000 per year			
	1964-66 (ref. 1)	1968-72 (ref. 2)	1973-77	1978-82
Oral cavity				
Tongue	14.0	12.6	10.2	9.7
Mouth (all other parts)	7.0	7.3	6.7	7.5
Pharynx				
Oropharynx	6.1 <sup>a</sup>	5.6	4.5	3.5
Hypopharynx	7.3	7.7	8.7	10.0
Digestive organs				
Oesophagus	13.0	15.2	14.7	15.0
Respiratory organs				
Larynx	13.8	13.6	12.4	10.1
Lung	13.3	13.5	14.7	15.8
All sites	139.5	143.1	142.1	147.4

<sup>a</sup>ICD 7, 145: tonsils and oral mesopharynx

log-linear polynomial of the first order, which is the usual model for analysing trends in cancer incidence (3). The average percentage change in incidence was obtained and the significance tested by Student's *t* test.

For cancers of the tongue, oropharynx and larynx, the average percentage changes in incidence were -4.39, -3.73 and -3.16, respectively, and these were highly significant (Fig. 1). For cancers of the hypopharynx, oesophagus and lung, the average percentage changes were 1.23, 0.95 and 0.05, respectively, and these were not significant (Fig. 2).

The decline in incidence of cancers of the tongue, oropharynx and larynx has been reported to be due to a cohort effect, younger five-year birth cohorts in general having lower rates than older cohorts (4). However, for cancers of the hypopharynx and oesophagus, no clear pattern was discernible; for lung cancer, there seemed to be no cohort effect at all (Fig. 3).

We considered that a synoptic measure of the experience of each birth cohort would lead

to better appreciation of the risk differentials between birth cohorts. On examining the age ranges for which the incidence data were available for each cohort, it was found that each cohort had two overlapping 15-year age intervals: one common to the five-year younger cohort and the other, common to the five-year older cohort. For example, the 1933 birth cohort had the age range 30-44 years common to the 1938 birth cohort and the age range 35-49 years common to the 1928 birth cohort (Fig. 4). Hence, a synoptic measure of risk in each birth cohort could be obtained by estimating the cumulative rate as defined by Day (5) over an appropriate age range. Accordingly, cumulative rates over an age range common to the five-year older or younger cohort were used to assess the risk differentials between adjacent cohorts.

A diagrammatic representation of cumulative rates in pairs of adjacent cohorts for the same age range is given in Figure 5 (4). It was observed that for cancers of the tongue, oropharynx and larynx, in each of the pairs of



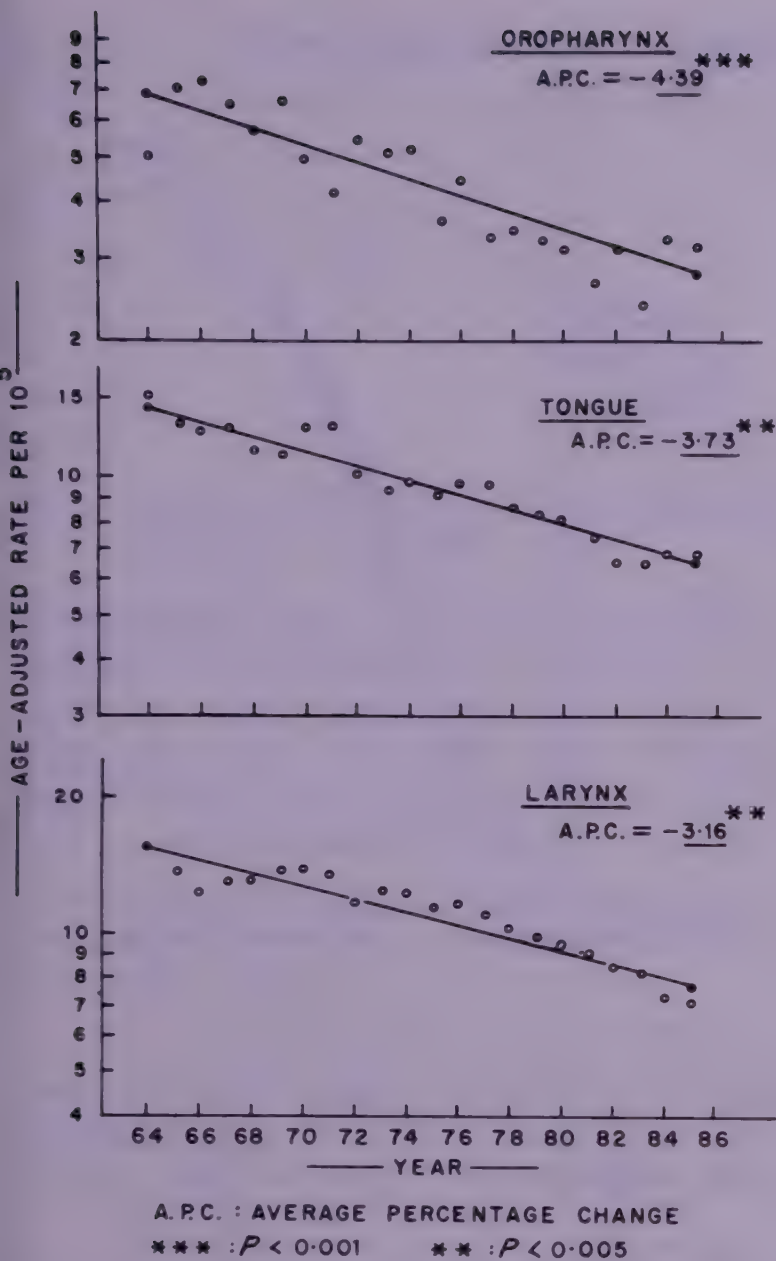


Fig. 1. Trends in age-adjusted incidence rates for cancers of the oropharynx, tongue and larynx in Greater Bombay, 1964-85

birth cohorts, the younger cohort had a lower cumulative rate. However, for cancers of the hypopharynx, oesophagus and lung, the pattern was not consistent; only cohorts born after 1928 seemed to have rates lower than those of five-year older cohorts, but for those born before 1928 the successive five-year younger cohorts had either similar rates or showed a reversal (i.e., younger cohorts having higher rates).

### INTERPRETATION OF TRENDS

The observed changes in the incidence rates are not likely to be artefacts, as various indices

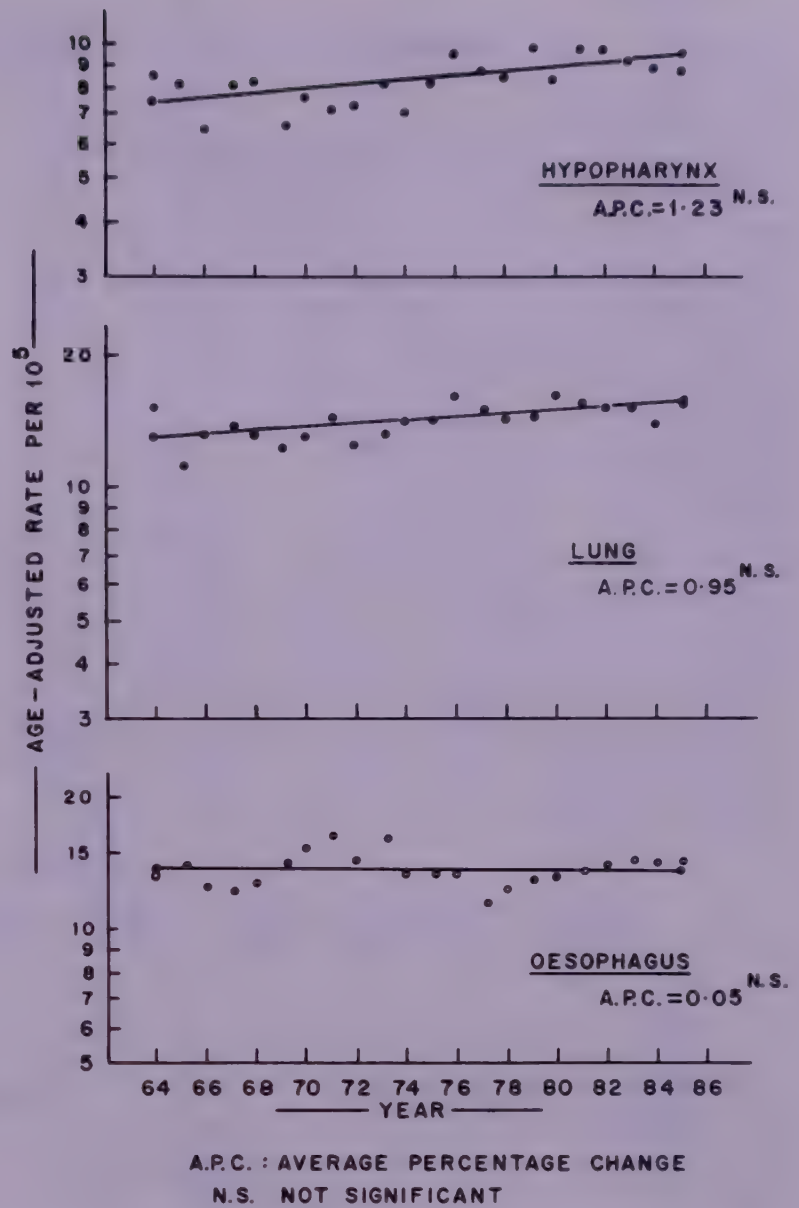


Fig. 2. Trends in age-adjusted incidence rates for cancers of the hypopharynx, lung and oesophagus in Greater Bombay, 1964-85

have shown that the data of the Bombay Cancer Registry are reliable (6). This changing pattern, therefore, needs to be viewed on the basis of changing exposure to etiological factors. For that purpose, it is essential to know the risk factors for cancers at each of the sites, the associated risk ratios and the prevalence of risk factors in the population over the years. It must be pointed out that most Indian oncologists pool cancers of the base of the tongue with cancers of the oropharynx, as it has been found that the clinical behaviour, prognosis and etiology of cancers of the base of the tongue are similar to those of

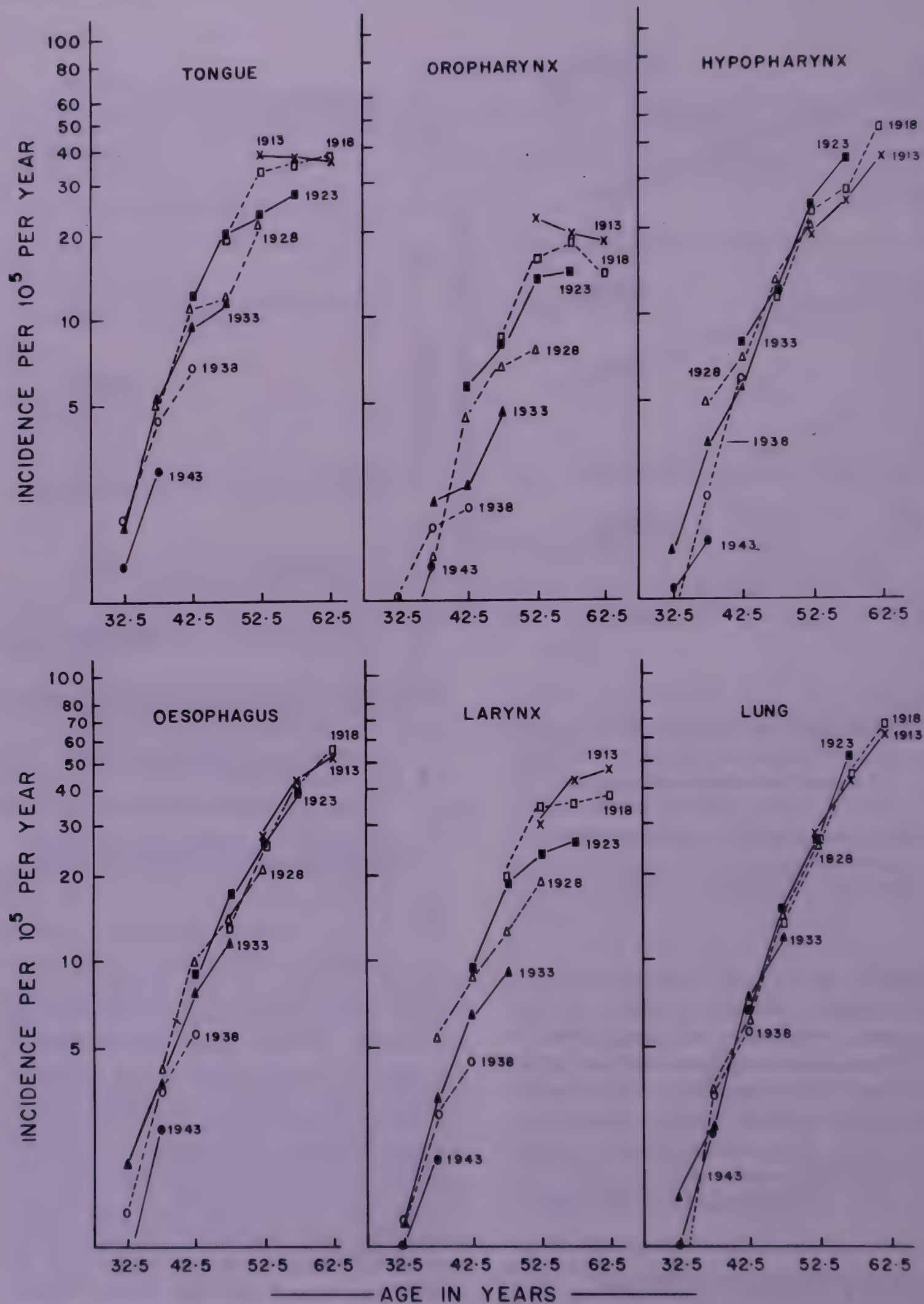


Fig. 3. Age-specific incidence of cancers of the tongue, oropharynx, hypopharynx, oesophagus, larynx and lung in cohorts born between 1913 and 1943



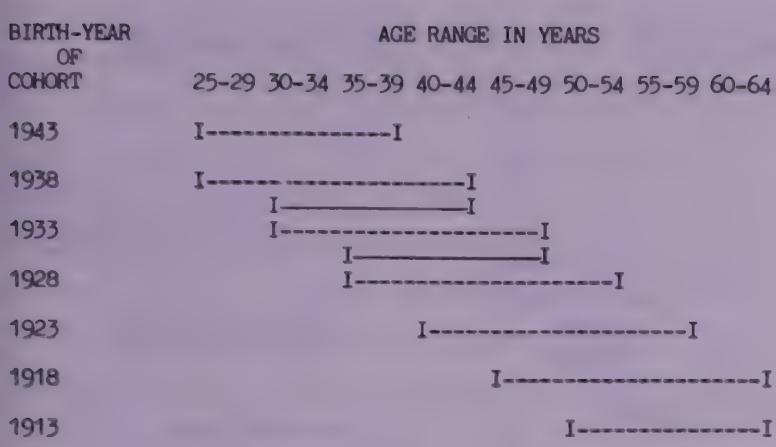


Fig. 4. Age ranges for which incidence data are available for various birth cohorts

oropharyngeal cancer (7). This practice is in contrast to the international classification, in which the entire tongue used to be grouped under one rubric. In Bombay, almost 75% of lingual cancers occur at the base of the tongue. It is therefore justifiable to consider that the risk ratio for cancer of oropharynx inclusive of the base of the tongue is appropriate for cancers of both the tongue and oropharynx.

The risk ratios obtained in a Bombay study for smokers and chewers as compared to nonusers of tobacco (8) are shown in Table 2. In this study, smokers who were

predominantly *bidi* smokers had strikingly higher risks of cancers of the oropharynx, including the base of the tongue (11.8) and larynx (7.7), than chewers (3.3 and 4.6, respectively). In contrast, chewers had a higher risk for cancers of the oral cavity (excluding the base of tongue) and hypopharynx (6.0 and 6.2, respectively). Smokers and chewers had similar risks for oesophageal cancer. Risks for oral, pharyngeal and laryngeal cancers specifically among cigarette smokers are not available from India. Two studies in the west showed that the risk ratios for oral cancers in cigarette smokers were about 1.5 (9) and 3 (10); the risk for cancers of the pharynx taken as a group was not significantly higher in smokers (11); for cancers of the larynx, the ratio was between 3 and 6, depending on the frequency of cigarette smoking (12).

It is interesting that *bidi* smokers have a much higher risk of cancers of the oropharynx and larynx compared to cigarette smokers. For cancer of the lung, *bidi* and cigarette smokers in Bombay had two- to three- fold higher risks (13). Furthermore, *bidi* smoking and tobacco

Table 2  
Risk ratios in smokers and chewers for tobacco-related cancers<sup>a</sup>

Site of cancer	Type of tobacco usage <sup>b</sup>			
	S	C	SC	CgS
Oral cavity excluding base of tongue	2.8	6.0	10.1	1.5-3.0
Pharynx				NS
Oropharynx, including base of tongue	11.8	3.3	31.7	
Hypopharynx	3.6	6.2	16.9	
Oesophagus	2.2	2.5	6.2	
Larynx	7.7	4.6	20.1	3-6 <sup>c</sup>
Lung				10-15
( <i>Bidis</i> )	3.4			
(Cigarettes)	2.4			

<sup>a</sup>Calculated from data in refs. (8-13)  
<sup>b</sup>S, smoker; C, chewer; SC, smoker-chewer; CgS, cigarette smoker  
NS, not significant  
<sup>c</sup>Risk ratios here refer to western studies

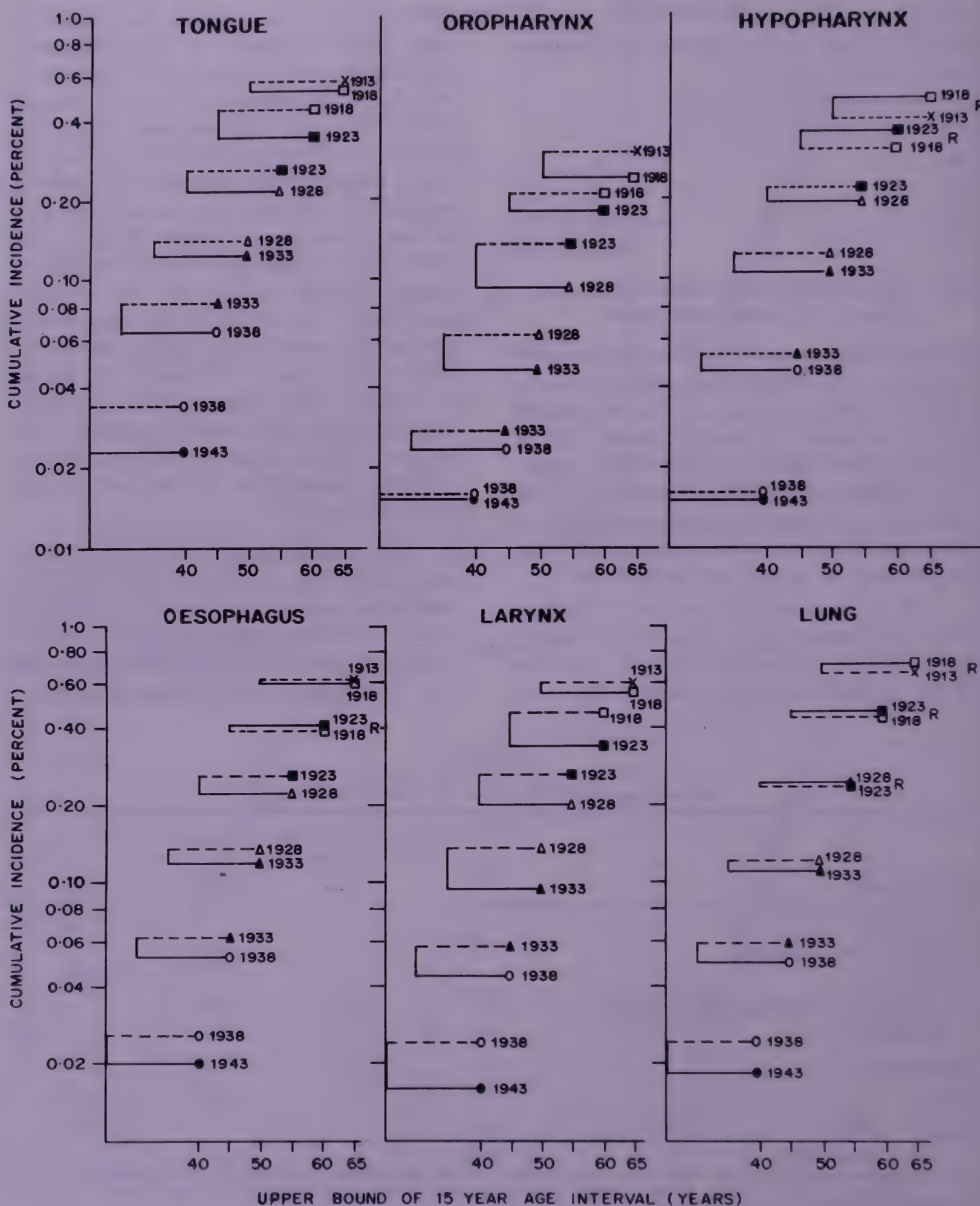


Fig. 5. Cumulative incidence rates over two overlapping 15-year age ranges for cancers of the tongue, oropharynx, hypopharynx, oesophagus, larynx and lung for various birth cohorts



chewing were found to be major risk factors for oral cancers and for cancers of the pharynx and larynx, and the risks attributable to tobacco usage were high, varying between 70 and 85%, depending on the site (14). Thus, the observed changes in incidence rates probably reflect the changes in tobacco usage that occurred in this population some 20 years ago. Data on the prevalence of tobacco usage in the population of Bombay over the years are not available to fully substantiate this hypothesis. An attempt to estimate the pattern of tobacco usage was made by considering limited data on prevalence by age available from a cohort study on blue-collar workers carried out in the 1970s (15). By approximating the habits in different age groups to the habit pattern in the corresponding birth cohorts, trends in the habits of cohorts born between 1921 and 1936 were assessed. These were used to interpret the cancer experience of cohorts born between 1913 and 1943.

Examination of the patterns in various birth cohorts showed a marked decrease in *bidi* smoking and a moderate increase in cigarette smoking in successively younger birth cohorts (Fig. 6). The pattern for those with dual habits, i.e., *bidi* smoking with tobacco chewing and cigarette smoking with tobacco chewing, is similar to that of people with the single habit of

smoking. This situation would lead to successive younger birth cohorts having lower incidence rates of cancers in which *bidi* smoking is the dominant risk factor. This may explain the trends in the incidence rates of cancers of the tongue, oropharynx and larynx, which are the major *bidi*-related cancers in this analysis.

Tobacco chewing remained more or less stable in various birth cohorts; and the incidence of oral cancer, excluding the tongue, for which tobacco chewing is the dominant risk factor, was also stable over the years. For lung cancer, for which both *bidi* and cigarette smoking are risk factors, and hypopharyngeal cancer, for which chewing is a more important risk factor than smoking, it is difficult to explain the lack of consistency in the pattern in successive birth cohorts; it is probably due to the paucity of data. Perhaps, detailed data on a representative sample of the entire population would provide a plausible explanation. For oesophageal cancer, the risk attributable to tobacco was only 50% (14), and no explanation of the trend (or rather lack of it) can be given solely on the basis of the prevalence of tobacco usage.

In order to assess whether the trends observed continue in the same direction, the latest five-year data were considered. Interestingly, the incidence rates for cancers of the oropharynx and larynx have stabilized, at about 3.5 and 10 per 100 000, respectively.

## FUTURE CANCER PATTERN IN THE COUNTRY

The pattern of tobacco-related cancers expected for the country as a whole on the basis of estimates of *per-caput* consumption of raw tobacco of different types, obtained from data published by the Ministry of Agriculture, is at variance with what was actually observed in Bombay (16,17). For instance, during the period 1951-81, the *per-caput* consumption of *bidi* tobacco increased from 145 to 191 g and that of cigarette tobacco from 55 to 115 g.

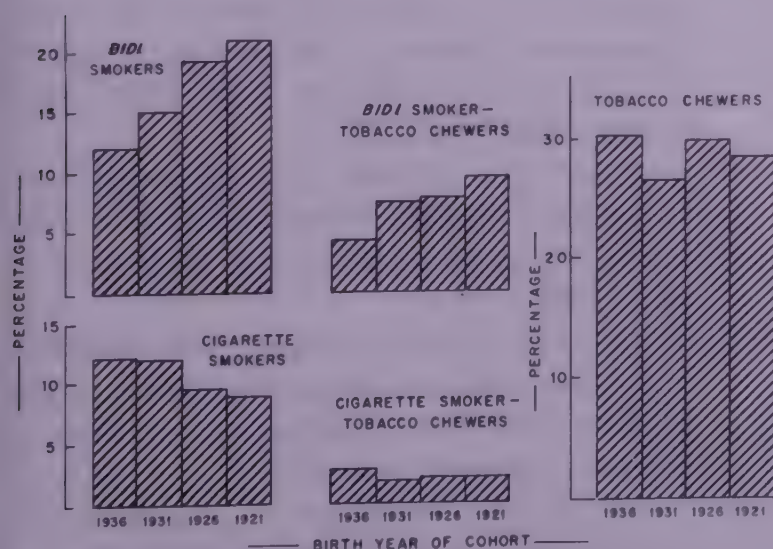


Fig. 6. Proportions of smokers and chewers in cohorts born between 1936 and 1921 (blue-collar workers in Bombay)



**Table 3**  
*Estimated per-caput consumption of raw tobacco (in grams) in India<sup>a</sup>*

Tobacco type	1951-52	1960-61	1970-71	1980-81
<i>Bidi</i>	145	168	155	191
Cigarette	55	97	133	115
Chewing	140	143	94	54
Total	556	566	474	541

<sup>a</sup>Calculated from data in refs. (16, 17)

Consumption of chewing tobacco, however, decreased from 140 to 54 g (Table 3). The possible implications are that the incidences of *bidi*-related cancers, i.e., cancers of the tongue, oropharynx and larynx, are unlikely to show a

decline in the near future. There is thus an urgent need to institute tobacco control programmes especially directed to all smokers in the country, with special emphasis on cigarette smokers.

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# Role of diet and alcohol in tobacco-related cancer at sites in the upper aerodigestive tract in an Indian population

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Cancers of the upper alimentary and respiratory tracts, for which tobacco is the major cause, constitute about one-third of all cancers among Indians. Probable changes in demography suggest that the incidence of these cancers will increase. Since a large segment of tobacco users remain cancer free, however, other factors may have a modifying effect on the risk of developing the disease. The modifying effect of diet on the occurrence of oral cancer was observed in an exploratory study in India in early 1970s. Subsequently, the role of various dietary factors and of alcohol were studied for cancers of all sites in the upper aerodigestive tract. The results indicate that intake of vegetables, fish and buttermilk (liquefied yogurt) was associated with a lower risk for upper aerodigestive tract cancers and that use of red chillie powder, a common spice used in Indian food, was a risk factor in a dose-dependent manner. Alcohol intake had a limited but significant influence on the risk for these cancers.

## INTRODUCTION

Epidemiological studies indicate that 80-90% of human cancers are attributable to environmental factors and life style. The major differences in the incidence rates of various cancers among different countries, between the genders, and between migrant and native populations, as well as time trends, implicate environmental factors in cancer causation.

In each country, there are characteristic site patterns of risk due to local exposure factors and life styles. For example, the rate of cancers at all sites combined among Indian males is quite low when compared with rates for men in Connecticut, USA, Oxford, United Kingdom, and Miyagi, Japan (1-6), where the incidence rates are two- to three-fold higher (Table 1). The incidence rates of cancers of the oral cavity, pharynx and larynx in India, however, are some of the highest in the world

(Table 1). The incidence of lung cancer, although low by international standards, is similar to that of oesophageal and pharyngeal cancers in the national context. Thus, in Indian males, cancers of the upper aerodigestive tract constitute 30-40% of all cancers, whereas they constitute only 12, 6 and 8% of cancers in Connecticut, Oxford and Miyagi, respectively. With the inclusion of lung cancer, however, cancers of the upper alimentary and respiratory tracts constitute 40-50% of cancer at all sites combined among Indian males and about 20% of cancers among Indian females.

The use of tobacco as a major risk factor for cancers at these sites is well established (7-10). Quantification of the risks associated with different tobacco habits has also resulted in high values. Even so, not all heavy chewers and smokers develop cancer; thus, it is likely



**Table 1**

*Average annual age-adjusted incidence rates of cancers of the upper alimentary and respiratory tracts in males per 100 000 population*

Registry	Oral cavity (140-145) <sup>a</sup>	Pharynx (146, 148)	Oesophagus (150)	Larynx (161)	Lung (162)	All sites combined (140-208)
<b>India<sup>b</sup></b>						
Ahmedabad	21.1	16.9	10.5	10.2	13.9	149.5
Bangalore	9.0	8.8	8.3	4.9	8.6	107.0
Bombay	13.4	11.8	11.4	8.0	13.8	120.5
Madras	12.0	6.8	7.4	4.9	7.5	91.1
Nagpur	15.3	9.7	14.1	13.1	8.6	122.2
Poona	14.8	5.7	12.8	11.2	11.3	127.6
<b>Others<sup>c</sup></b>						
Connecticut, USA	10.6	3.7	5.3	8.2	60.9	303.0
Oxford, UK	5.2	1.2	3.8	3.9	69.3	268.5
Miyagi, Japan	1.9	0.4	13.8	2.2	25.5	208.9

<sup>a</sup>Figures in parentheses are ICD codes: 9th for Indian registries; 8th for other registries, with codes 140-207 for all sites instead of 140-208

<sup>b</sup>Source: refs. (1-5)

<sup>c</sup>Source: ref. (6)

that certain secondary factors, either external or internal, may have modifying influences on the risk, and diet and nutrition could be one such factor. This paper reviews the role of diet and also of alcohol in the pathogenesis of cancers of the upper aerodigestive tract.

## ROLE OF DIETARY FACTORS

Nutrition and diet can act in several ways. Nutrients, food additives and contaminants (like aflatoxins) can act as complete carcinogens or pro-carcinogens. Dietary deficiencies or excesses can lead to biochemical malfunction, which in turn may initiate or promote a neoplastic process; they may also impede or enhance the delivery of carcinogens to the target tissue. They can result in metabolic activation or deactivation of carcinogens. Thus, diet and nutrition can interact with the host environment in several ways and alter the susceptibility of tissues to cancer induction and promotion (11). Generally, several dietary components are considered to act more as

tumour promoters or antipromoters rather than as direct carcinogens.

An exploratory analysis of data collected in the 1950s in Bombay, India, indicated that certain dietary components may modify the risk of tobacco chewers and smokers for developing oral cancer (12). This formed the basis for a case-control study (13) conducted subsequently for all sites in the upper aerodigestive tract. Some of the results abstracted from this study are discussed below.

## DIET AND CANCERS OF UPPER AERODIGESTIVE TRACT

Cancers of the oral cavity, pharynx, larynx and oesophagus formed the case group for this study. Two control groups were used. The results obtained with controls from the general population (using electoral rolls) are shown in Table 2. Information on usual diet before disease onset, in terms of the frequency and amount of intake, was obtained by a



Table 2

Relative risk estimates for cancers of the upper aerodigestive tract (with 95% confidence intervals) associated with consumption of different dietary items in Bombay, India<sup>a</sup>

Dietary item (level of comparison)	Cancer site			
	Oral cavity	Pharynx	Oesophagus	Larynx
<b>Cereals and pulses</b>				
Cereals	1.45	1.59	1.51	0.87
(not daily <i>vs.</i> daily)	(0.8-2.5)	(0.9-2.9)	(0.9-2.7)	(0.4-1.9)
Pulses	1.57	1.90	1.11	1.48
(not daily <i>vs.</i> daily)	(1.0-2.5)	(1.2-3.1)	(0.7-1.8)	(0.8-2.8)
<b>Vegetables and fruits</b>				
Vegetables	2.39	2.65	2.62	2.75
(not daily <i>vs.</i> daily)	(1.4-4.0)	(1.6-4.5)	(1.5-4.4)	(1.4-5.3)
Fruits (<1/week <i>vs.</i> ≥1/week)	0.89	0.99	1.23	2.00
	(0.5-1.4)	(0.6-1.6)	(0.8-2.0)	(1.0-4.1)
<b>Animal products</b> (<1/week <i>vs.</i> ≥1/week)				
Meat	1.21	1.13	1.46	1.12
	(0.7-2.0)	(0.7-1.9)	(0.9-2.5)	(0.6-2.1)
Fish	3.28	2.23	3.77	3.94
	(2.1-5.3)	(1.3-3.7)	(2.3-6.3)	(2.1-7.7)
Poultry	0.78	0.90	3.50	1.12
	(0.1-5.2)	(0.1-7.0)	(0.3-48.9)	(0.02-48.3)
Eggs	0.83	0.43	0.79	0.64
	(0.5-1.5)	(0.2-0.8)	(0.4-1.4)	(0.3-1.4)
<b>Dairy products</b> (not daily <i>vs.</i> daily)				
Milk	1.11	1.13	1.47	0.78
	(0.6-2.2)	(0.6-2.3)	(0.7-3.0)	(0.3-2.0)
Buttermilk	3.71	3.68	2.44	11.09
	(1.6-8.7)	(1.4-9.4)	(1.1-5.4)	(1.5-83.1)
<b>Fat</b>				
Groudnut oil (g/cu/month)	2.91	2.93	1.99	2.61
(<600 g <i>vs.</i> ≥ 600 g)	(1.8-4.7)	(1.8-4.8)	(1.2-3.2)	(1.3-5.1)
<b>Spices</b>				
Red chillie powder (g/cu/month)				
< 75	1.00	1.00	1.00	1.00
75-99	2.61*	1.45	1.94	1.22
100-149	3.79**	2.33	1.99	2.05
≥ 150	3.94**	2.37**	2.85**	3.39**
χ <sup>2</sup> trend test	<0.001	<0.01	<0.01	<0.10
<b>Beverages</b>				
Tea	1.21	1.46	2.39	1.10
(>2 cups/day <i>vs.</i> ≤ 2 cups/day)	(0.8-1.9)	(0.9-2.4)	(1.5-3.9)	(0.6-2.0)

<sup>a</sup>Source: ref (13): Comparison group; general population

Relative risk adjusted for age and tobacco use

\**p* < 0.05; \*\**p* < 0.01

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questionnaire. Findings from the analysis based on the frequency of intake of several dietary items (13) are summarized in the table. The results are given in terms of relative risk estimates that were adjusted for the two important risk factors, use of tobacco and age. Adjustment was not required for sex or community, as all the patients were men and they belonged to one community with similar socioeconomic status.

**Cereals and pulses:** These constitute the most common food items for all segments of the Indian population. Table 2 compares the risks of those who did not consume these items daily *versus* those who did. For those who did not include pulses in their diet daily *versus* those who did, the relative risk (1.9) was significant for pharyngeal cancer.

**Vegetables and fruits:** A two- to three-fold increase in risk was observed for men who did not consume vegetables daily *versus* those who did, and these were highly significant. The lower risks were consistent with the current hypothesis that vitamin A,  $\beta$ -carotene and vitamin C have protective effects. Intake of fruits, however, showed no association; this was not surprising, since both the control and study groups were from the lower income stratum and, perhaps understandably, could not afford this relatively expensive food item.

**Animal products:** Risks were also assessed for men who ate meat, fish, poultry and eggs less than once a week *versus* those who consumed these items at least once a week. Only fish intake showed a significant relative risk, which was two- to four-fold higher for nonconsumers than consumers.

**Dairy products:** Milk intake was found to be relatively poor in both the study and control groups, and the relative risks were not significant. Butter was consumed by only 0.2% of the study group and was therefore not analysed. Nonconsumers of buttermilk (liquefied yogurt) were at significantly higher risk than consumers.

**Fat:** Information was obtained on the consumption of various types of fats and oils, and the quantity consumed was expressed in grams per consumption unit (cu) (one for a member of the family 12 years of age and above, half otherwise) per month (g/cu/mth). Groundnut oil was the most commonly used cooking medium (81-86% in different groups), and median consumption in the population control group was 600 g per cu per month while that of the whole study group was 400 g per cu per month. Men who consumed less oil were at a two-fold higher risk than those who used more. In contrast to the western diet, in which fat contributes 30-40% of the total caloric intake, in an average Indian diet fat consumption is low and contributes only 8-10% of the total caloric intake. High fat consumption in western countries was reported in several studies to be associated with higher risks for cancers of the colon and of endocrine-dependent sites (14,15); so the risk elevation even with low caloric intake from fat in this study is interesting.

**Spices:** Red chillie powder is an important spice in Indian food, and this emerged as a risk factor in a dose-dependent manner. With an increase in chillie use from <75 g to 150 g or more per cu per month, there was a one- to three-fold increase in risk, which was significant for all sites except the larynx. This observation is consistent with experimental findings that red chillies are mutagenic in bacterial test systems and are tumour promoters *in vivo* (16,17).

**Beverages:** Barely 2% of the study group drank coffee, but drinking of tea was common, the median intake being two cups per day. There was a significant, two-fold increase in risk for oesophageal cancer among men who drank more than two cups of tea a day as compared to those who drank two cups or less. For pharyngeal cancer, the risk was 1.5, which was only marginally significant.

When men who drank three, four, five or more cups of tea per day were compared with



those who drank two cups or less per day, a significantly increasing trend of relative risk for oesophageal (2.0, 2.2 and 3.5) and pharyngeal cancers (1.1, 1.8 and 2.3) was observed. It is possible that it is the temperature of the tea and not the tea itself that is relevant, but it was not possible to study this aspect in our investigation.

Since this is the only case-control study on diet and cancer in India, the results need to be interpreted with caution. Furthermore, it was not possible at this stage to assess the attributable risks due to dietary factors, as has been done for tobacco (18).

## DISCUSSION

A number of studies have reported similar results. In an extensive study by the International Agency for Research on Cancer, the role of several food items was investigated in the induction of oesophageal cancer in an area of high incidence (165 per 100 000) in Iran. Of the 45 food items listed (19), nine showed a significant association with the disease in both males and females. Tea drinking was one of them; a significant, almost two-fold increase in risk was observed among those who drank hot tea compared to those who did not. The other items included consumption of dairy products, raw vegetables and fruit; these were found to have a significant protective effect, the risks for higher *versus* lower levels of consumption ranging from 0.42 to 0.69. Consumption of meat, poultry and fish showed no association, nor was there a significant association with tobacco use or alcohol intake.

In a case-control study on oral and pharyngeal cancers in women in the southern USA, Winn *et al.* (20) reported a significant protective effect of vegetable and fruit consumption. A report from the Roswell Park Memorial Institute (USA), where large-scale questionnaire studies on diet are routinely conducted, also revealed a protective effect of vegetable and fruit intake, but not of meat or

fish intake, on the development of oesophageal cancer, in a dose-dependent manner (21). Using standard food composition tables, it was shown that higher dietary levels of vitamins A and C conferred protection. A similar protective effect of vitamins A and C was reported for laryngeal cancer (22), and the gradient in risk persisted even after adjustment for the effects of alcohol drinking and cigarette smoking.

It is not easy to quantify the contribution of diet to cancer risk because of the complexity and extreme difficulty of measuring in meaningful quantitative terms dietary intake prior to disease onset. Moreover, dietary items interact not only with each other but also with the host environment. Despite these complexities, certain consistent associations with specific food items have been observed.

It may be concluded that, although tobacco is known to be a major causal factor for some human cancers and efforts must be made to eliminate its use, the tumour promoting or protective role of certain dietary factors cannot be ignored. It is therefore suggested that a balanced diet adequate in protein and nutrient intake, especially fresh vegetables and fruits rich in minerals and vitamins, coupled with avoidance of high intake of fats and meat and strict surveillance of quality, preservation and storage practices, would be consistent with the lowest possible risk for cancer and other diseases for the Indian population.

## ROLE OF ALCOHOL

Alcohol plays an important role in the pathogenesis of cancers of the upper alimentary tract, especially in conjunction with cigarette smoking. In the present study, alcohol was consumed in the form of a locally distilled brew.

The risks of alcohol drinking and tobacco smoking and chewing were assessed using log-linear models, which were translated into logistic regression models for the dichotomous response variable (23). Table 3 shows the



**Table 3***Estimates of odds ratios associated with regular habits obtained under fitted logistic models<sup>a</sup>*

Adjusted odds ratios associated with	Cancer site		
	Oral cavity	Pharynx	Oesophagus
Smoking	7.4	5.6	4.7
Chewing	11.4	6.8	4.9
Alcohol drinking	1.3	2.2	<sup>b</sup>

<sup>a</sup>Source: ref. (23): Comparison group; general population controls<sup>b</sup>Because of an age-alcohol interaction term in the model, estimates of odds ratios differ with age group and are 2.7, 2.6 and 0.6 for age groups 40-49, 50-59 and  $\geq 60$  years, respectively.

results abstracted from this study. The risks associated with alcohol intake *per se* were not as high as those associated with tobacco habits; for oral cancers, the adjusted odds ratio of regular chewers was 11.4, and that for regular smokers was 7.4, while for alcohol consumers it was only 1.3. Similarly, for pharyngeal cancers, the risk associated with alcohol drinking was lower than those associated with tobacco habits. Because of the presence of an age-alcohol interaction term in the model fitted for oesophageal cancer, a single risk figure could not be obtained; these varied from 0.6 to 2.7 in different age groups. The risks for a combination of habits can be obtained by multiplication, and they are high. In another study of oesophageal cancer from this region (24), similar risks were reported.

Pure ethyl alcohol is not likely to be carcinogenic to man, since studies in animal systems have invariably given negative results; but the possibility cannot be ruled out. Contaminants in alcohol might, however, play a role in the pathogenesis of cancer. It has been suggested that the mechanism of the alcohol-cancer association may be related to nutritional deficiencies, which would increase susceptibility to the carcinogenic potential of an external agent like tobacco. Alcohol may also act as a solvent and enhance penetration of carcinogens into target tissues (25). Although the effect of alcohol in inducing cancers of the upper alimentary tract has been demonstrated in several epidemiological studies, its mode of action in the carcinogenic process is still not clear.

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# Maternal smoking and childhood mortality and morbidity

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Maternal smoking during pregnancy leads to a higher infant mortality by increasing several risks including that of low birthweight. About 10% of infant deaths and 19% of low birthweights of babies could be prevented in the USA if smoking by mothers during pregnancy could be eliminated. Our research documents that 22-31% of very 'low birthweight' births, 17% of childhood asthma and 38% of childhood asthma requiring medication could be prevented if maternal smoking were eliminated. Controlling for many confounding factors indicates that the effects of smoking are relatively independent of other known risks. Maternal smoking also appears to be related to subsequent behavioural problems of young children. Unfortunately, there is a lack of effective smoking cessation services during pregnancy in the USA, thus missing a clear opportunity to reduce substantially both infant mortality and childhood morbidity.

## INTRODUCTION

The impact of cigarette smoking on the health of smokers has been well documented. In this paper, we examine the impact of maternal smoking on a wide spectrum of indicators of the health status of infants and children, utilizing published studies as well as new research findings. Smoking by mothers can affect the fetus during pregnancy *via* an intrauterine pathway or after childbirth through passive smoking *via* an airborne pathway or breast feeding. These results have important implications for maternal and child health policies and programmes in many countries. Not only is there substantial evidence for the adverse effects of maternal smoking on the health of infants and children, but the preventable nature of the habit and the magnitude of attributable risks indicate that smoking by mothers is the greatest single preventable

cause of infant and childhood mortality and morbidity in the USA and numerous other countries (1).

These relationships are particularly important at this moment because of recent evidence that infant mortality rates in the USA are levelling off (2,3). In addition, there has been little change in the rates of low birthweight in the USA since the 1950s. In recent decades, there has been a very substantial impact of neonatal intensive care technology in reducing the rates of mortality and subsequent morbidity among infants in the USA. The lack of change in these rates points to the need to look beyond medical high technology to other intervention strategies to reduce further excess mortality and morbidity. Evidence from other countries including India indicates widespread use of tobacco (both smoked and chewed) and substantial infant health risks (4,5); similar



policy implications need to be addressed in these countries.

Smoking cessation programmes for pregnant women and all mothers and fathers with children represent one obvious strategy. At this point, it is unknown to what extent prenatal care services in the USA have an impact on maternal smoking cessation during pregnancy. There is perhaps a clear opportunity to reduce substantially both infant mortality and childhood morbidity by implementing effective cessation programmes during the prenatal period.

Similar opportunities may exist in many developing countries where tobacco use by pregnant women is widespread. While other causes of infant ill-health in these countries may be more dominant, for example, malnutrition, poverty and diarrheal disease, the cost-effectiveness of smoking cessation *versus* other health programmes can be assessed.

## METHODS

**Low birthweight and smoking:** To study the effect of maternal smoking on birthweight, the 1980 National Natality Survey (NNS) and Mississippi and Maine Multi-State Infant Mortality Review Project data were used. The NNS was carried out by the National Center for Health Statistics and was based on a random sample of 9941 live births to residents of the USA in 1980. Infants with a birthweight of less than 2500 g were oversampled. Information was derived from the birth certificate and a mailed questionnaire (a telephone interview if the mailed questionnaire was not returned) from all married mothers; the study also included data from hospital and physician records. The analyses excluded women not married at the time of the interview (6). The overall response rate to the survey was 84% (7). Information on smoking during pregnancy and other risk factors was gathered as part of the mailed/telephone questionnaire administered to the women.

Data were collected as part of the Multi-State Infant Mortality Review Project during 1984-85 in the entire State of Maine and two health districts in Mississippi. Data from Maine consisted of vital records and medical record audit data for all infant deaths, all survivors of very low birthweight, and a 2:1 random sample of controls or births matched on date of birth and plurality. Similar data were collected from the health districts in Mississippi. Data on smoking were abstracted from a detailed review of the medical records. Analysis of the Multi-State data reveals rates of smoking during pregnancy similar to, although slightly lower than, rates estimated from national samples. Rates for white women (both married and unmarried) who smoked during pregnancy in Maine (24%) and Mississippi (27%) were similar to the rates reported in the NNS (27%) and in a recent national sample (27%) (6); rates among black women in Mississippi (12%) were lower than NNS estimate (22%) and the recent national estimates (24%) (6). Lower estimates in the Multi-State study could be due to true differences in smoking or underreporting on the clinical record.

**Maternal smoking and behavioural problems in children:** Data from the 1981 National Health Survey and Child Health Supplement were used to analyse maternal smoking and behavioural problems in young children (aged 4-5). The National Health Survey uses a complex, multi-stage probability sampling design to provide representative samples of the civilian non-institutionalized population of the USA. The 1981 survey included a child health supplement, in which data were collected on one child in each eligible household thus including 1279 children aged 4-5 years. The interview contained a series of questions on parent-reported behavioural problems of the child (the Behaviour Problem Index, BPI), maternal behaviour relating to the prenatal experience of that child and sociodemographic measures. Thus, all information was derived



from reports of parents; there were no medical examinations of children or reviews of medical or school records.

The BPI was developed to encompass domains of behaviour similar to those covered by the Achenbach Child Behaviour Checklist (CBCL), but it was much shorter. Most items used in the BPI were adapted from the parent-administered CBCL, and they were chosen because of their reliability, high loading on the subscales of the CBCL and their adaptability to an interview situation. The CBCL has been validated, and it discriminates between children who are referred for clinical help for behavioural problems and children who are not referred. The BPI also discriminates between children who are and are not receiving help from psychologists, psychiatrists or psychoanalysts (8).

The BPI scales in this sample include an overall behavioural problem score and six subscales. In computing scale scores, each behavioural question was coded '1' if the parent said 'often true' or 'sometimes true' and was coded '0' otherwise. These recodes were then summed to give total and subscale scores. The scale items were designed to represent measures of some of the 'common syndromes of problem behaviour found in children and adolescents'. The subscales included the following (sample items in parentheses): (i) headstrong ('is disobedient at home'); (ii) antisocial behaviour ('bullies, or is cruel or mean to others'); (iii) anxious/depressed ('is unhappy, sad, or depressed'); (iv) hyperactive behaviour ('has difficulty concentrating, cannot pay attention for long'); (v) peer conflict-social withdrawal ('has trouble getting along with other children'); and (vi) immature dependency ('cries too much').

**National estimates of smoking and prenatal care:** National estimates of smoking during pregnancy and utilization of prenatal care services were derived from the 1980 NNS. When calculating population prevalences, estimates

were weighted to take into account the probabilities of selection, response rates and non-response. The prenatal care index was calculated to adjust for the number of visits during gestation: inadequate care included either late initiation of care or few visits (adjusted for gestation).

## RESULTS

**Maternal smoking and low birthweight, prematurity and intrauterine growth retardation:** Of all the potentially changeable risk factors that have been linked to low birthweight, cigarette smoking stands out as the one that has been well documented in its effects upon rates of low birthweight, prematurity and intrauterine growth retardation. A world literature review by Kramer (1) indicated the importance of smoking during pregnancy as a major health issue in all countries where the habit is prevalent among pregnant women. In addition, he pointed to the importance of tobacco chewing among pregnant women in countries where this habit is practised.

A significant relationship between smoking during pregnancy and rates of low birthweight and very low birthweight were found among married women in the NNS. In a logistic regression analysis controlling for prepregnancy weight, stature, prior pregnancy loss, maternal education, race and the adequacy of prenatal care, the rates of low birthweight were 2.1 times higher for women who smoked more than half a pack of cigarettes per day ( $p < 0.00001$ ) (Table 1). Similar relationships were found between smoking during pregnancy and low birthweight infants delivered prematurely (less than 37 weeks), as well as low birthweight infants delivered at term (37 weeks) or later, which we classify as intrauterine growth retardation.

The NNS sample indicated whether women had smoked prior to their pregnancy, and thus the relationship between smoking cessation during pregnancy and birth outcomes could be assessed. Weighted logistic



**Table 1**

*Estimated odds ratios of low birthweight from logistic regression analysis; 1980 National Natality Survey (n=7766)*

Predictive variable and categories	Odds ratio <sup>a</sup>	p-value
<b>Maternal weight</b> (approx. quintiles)		
1	1.74	0.00001
2	1.47	
3	1.22	
4	1.02	
5	1.00	
<b>Short maternal height</b>		
No	1.00	0.0001
Yes	1.40	
<b>Prior pregnancy loss</b>		
None	1.00	0.00001
One	1.61	
Two or more	1.97	
<b>Mother's education</b>		
Less than high-school	1.25	0.03
High-school diploma	1.09	
Some college	1.00	
<b>Race</b>		
White	1.00	0.00001
Black	2.24	
<b>Smoking during pregnancy</b>		
>1/2 pack per day	2.10	0.00001
≤1/2 pack per day	1.60	
None	1.00	
<b>Prenatal care index</b>		
Inadequate	2.30	0.00001
Intermediate	1.48	
Adequate	1.00	

<sup>a</sup>Odds ratios independently associated with a low birthweight, relative to the reference category (which has a value of 1.00)

regressions were estimated, and these indicated the same level of risk for those women who quit (did not smoke during pregnancy) as for those who had not smoked prior to or during pregnancy. Relatively low cessation rates during pregnancy were observed in the NNS: 16% among whites and 11% among blacks.

Previous studies have not documented a clear relationship between rates of very low birthweight (<1500 g at birth) and smoking during pregnancy. Analysis of the NNS and data from the Maine and Mississippi Multi-State studies indicate a substantial relationship (Table 2).

Estimates of attributable risk from studies of the NNS data indicate that elimination of smoking among white, married women could reduce rates of low birthweight by 19% (7). We expect similar attributable risks among the black population.

Attributable risks estimated from the NNS and Multi-State data indicate that eliminating smoking during pregnancy could decrease the rates of very low birthweight by 15%.

**Maternal smoking and infant mortality:** While the relationship of maternal smoking during pregnancy to low birthweight, prematurity and intrauterine growth retardation has been clearly documented in a wide variety of studies throughout the world, the relationship of smoking during pregnancy to infant mortality has been less clear. Studies completed one or two decades ago reported conflicting results (9-11); however, more recent results based on much larger sample sizes indicate substantial effects upon infant mortality *via* both increased risk of low birthweight and other risks independent of birthweight (12, 13). These results are consistent with the effects of passive smoking both *in utero* and following childbirth (13). Estimates of attributable risk indicate that 10% of infant deaths could be prevented if mothers did not smoke during pregnancy (12).

**Maternal smoking and respiratory health of children:** A substantial body of literature demonstrates increased rates of lower respiratory infection and increased respiratory symptoms in the children of mothers who smoke (14-18). Other studies indicate an association between maternal smoking and diminished



Table 2

Estimated odds ratios of very low birthweight, controlling for prior pregnancy loss, race and lack of prenatal care, 1980 National Natality Survey (NNS) and 1984-85 Multi-State Maine and Mississippi samples

Risk	Multi-State					
	NNS (n=7825)		Maine (n=1017)		Mississippi (n=902)	
	Odds ratio	p-value	Odds ratio	p-value	Odds ratio	p-value
Unadjusted odds; smoking <i>vs</i> not	1.77	0.0001	1.46	0.01	1.34	0.12
Controlling for prior pregnancy loss and race (only NNS and MS)	1.68	0.0001	1.59	0.004	1.39	0.11
As above plus lack of prenatal care	1.62	0.0003	1.49	0.06	1.43	0.09

lung size (19) and decreased pulmonary function (20-30).

A recent study from our research group indicated a substantial association between maternal smoking during pregnancy (0.5 packs per day or more) and an increased risk of asthma among children aged 0-5 (31), similar to results from an earlier study of passive maternal smoking (32). These results were obtained from a multivariate logistic regression analysis controlling for sex, race, family structure, rooms in household and maternal education (odds ratio, 2.1;  $p<0.001$ ). Similar analyses indicated that maternal smoking of 0.5 packs per day or more was also an independent risk factor for children's use of physician-prescribed asthma medications (odds ratio, 4.6;  $p<0.0006$ ) and for developing asthma in the first year of life ( $p<0.0006$ ) (29). The mechanisms by which maternal smoking may cause an increased risk of childhood asthma is unclear. Most of the studies have assumed an effect of postnatal passive smoking, but some newer studies indicate that exposure during pregnancy might have independent effects, by impairing lung development and by sensitization to atopic disease (33, 34).

**Maternal smoking and later behavioural problems in children:** Nicotine, the active agent in tobacco which leads to addiction,

exhibits a wide variety of effects on the human body: (i) nicotine enters the brain, interacts with specific receptors in brain tissue and initiates metabolic and electrical activity; and (ii) nicotine causes skeletal muscle relaxation and has cardiovascular and endocrine (i.e., hormonal) effects (35). Exposure to nicotine, *via* passive smoke, breast feeding or intrauterine routes, might have behavioural consequences for children.

In a recent analysis of national data in the USA, we found a significant relationship between particular behavioural problems reported by parents and maternal smoking during pregnancy. The BPI contains six subscales and an overall summary score (see above). In a multiple regression analysis, we controlled for gender of the child, birthweight, race, region of the country, mother's age at childbirth, number of siblings, family structure, family income and mother's education. For the overall BPI, a weak independent relationship was indicated between maternal smoking and behavioural problems ( $p=0.07$ ). The 'antisocial' subscale also showed a weak relation to maternal smoking ( $p=0.06$ ), while the 'headstrong' subscale showed a more substantial, independent relation ( $p=0.008$ ).

These results, although preliminary, are intriguing, because the relationships seen in



these analyses are of the same order of magnitude as relationships to other established risk factors for behavioural problems, such as male gender. The present study had a retrospective design, and, obviously, cohort and intervention (e.g., smoking cessation) studies are needed to further test these hypotheses. A recent longitudinal analysis has found stronger relationships (36).

**Smoking cessation during pregnancy and prenatal care: Is there a connection?** Substantial relationships were observed between lack of prenatal care and increased rates of low birthweight in the NNS (Table 1). These analyses demonstrated independent relationships between low birthweight and smoking, and between low birthweight and inadequate prenatal care.

These independent associations were not unexpected. In addition we found that smoking was related to adequacy of prenatal care. One of the mechanisms whereby prenatal health care has been hypothesized to improve birthweight is *via* counselling and support to women to quit smoking. Some 31% of women with inadequate prenatal care smoked during pregnancy *versus* 25% of women with adequate prenatal care ( $p < 0.002$ ). Rates of smoking cessation were also different (9% *vs.* 17%;  $p = 0.002$ ).

## IMPLICATIONS

The evidence for the harmful effects of maternal smoking on the health of the newborn is now substantial. Our review of published

evidence, as well as new data, indicate widespread effects of maternal smoking upon mortality and morbidity. Randomized controlled trials indicate the effectiveness of smoking cessation programmes during pregnancy in helping women quit (37, 38) and in improving birthweight (39). Unfortunately, such programmes are not widespread. The problem in the USA at this point seems to be one of devising a reimbursement mechanism that would allow a diversity of low-cost programmes, most of which would not be carried out by physicians although physician reinforcement is important. Insurance and Medicaid programmes in the USA generally do not provide reimbursement for smoking cessation programmes during pregnancy. Evaluation of these interventions is critical.

Application of this relatively recent scientific knowledge to other populations throughout the world also needs to be explored. Other systems for delivering nicotine, such as tobacco chewing; must be examined for their effect upon infant and child health. Finally, new programmes of smoking cessation must be developed and evaluated in these countries. A key issue in this evaluation is the development of low-cost, effective systems which can be integrated into routine prenatal and postnatal care.

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# Population impact of adverse reproductive outcome attributable to maternal tobacco use in India

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The prevalence of tobacco use among women in India ranges from 10 to 62%. Tobacco is used by women predominantly in its smokeless forms; overall, an estimated 10% of Indian women chew tobacco and 2.5% smoke *bidis*. Nevertheless, the potential health hazards of maternal tobacco use to reproductive outcome are not well documented. Preliminary estimates showed a three-fold risk of stillbirths among women in India who chewed tobacco during pregnancy and a two-fold increase in perinatal mortality for babies born to *bidi* smokers in Bangladesh. The odds ratio for low birthweight (2.5 kg or less) associated with *mishri* use during pregnancy was 3.2 for all babies in Bombay, 6.96 for girls and 1.6 for boys. From these estimates, about 17% of stillbirths, 9% of perinatal mortality and 17% of birthweights of 2.5 kg or less are attributable to maternal tobacco use during pregnancy. Estimates for 1986 showed that nearly 457 000 deaths among infants and children under five years could be attributed to maternal tobacco use. Additional indirect effects may be increased infant mortality due to premature birth and diversion of income from nutritional needs to tobacco. These estimates emphasize the necessity for stopping tobacco use during pregnancy and the need for appropriate antenatal efforts.

## INTRODUCTION

Maternal cigarette smoking is harmful to the unborn fetus, newborn, neonate and growing child in various ways. Cigarette smoking during pregnancy adversely affects the growth of the unborn fetus, resulting in low birthweight, increased numbers of stillbirths and increased perinatal, neonatal and infant mortality (1). It is also associated with a decrease in the male:female ratio of newborns (2,3) and with an increased prevalence of infections (4). Further, it slows or adversely affects the respiratory, mental, emotional and behavioural development of the child at newborn, infant, under-five and over-five stages (1,4).

Tobacco is used in various forms throughout India and South-East Asia (see papers by Bhonsle *et al.*; Pindborg *et al.*; this volume), but

very little is known about its adverse effects on pregnancy, a topic which has been reviewed recently (5,6). Studies from Pune (7) and Jabalpur (8) in India and from Bangladesh (4) showed that maternal tobacco chewing (7,8) and *bidi* smoking (4) during pregnancy result in offspring of low birthweight. A three-fold increase in the number of stillbirths was seen among tobacco chewers (7), and increased placental weights were also reported (9,10). A two-fold increase in perinatal mortality was associated with *bidi* smoking (4). Perinatal mortality was twice as high among illiterate and less well educated women than among educated women and among those who had had little or no antenatal care compared to those who had sought antenatal care. Less well educated women were more likely to be *bidi* smokers and to have sought no or less



antenatal care. Thus, lack of education, *bidi* smoking and lack of antenatal care seem to be interrelated. Furthermore, the scarce income of poorer, less well educated women may be diverted from nutritional and other needs to the purchase of tobacco (11), which would add indirectly to the adverse effects of tobacco.

Relative risk estimates for the effects of maternal use of smokeless tobacco during pregnancy are available from a preliminary study in Bombay, India (12). In this study, 33% of the 500 women were *mishri* users, and they had a nearly three-fold greater risk of bearing an offspring with low birthweight (2.5 kg or less) than nonusers of tobacco. Female babies had a nearly seven-fold risk of weighing less than 2.5 kg ( $p < 0.0005$ ); for male babies, the birthweights showed no significant difference. The relative risk for having a baby weighing 2 kg or less was 5.4, and that for having a baby weighing 2-2.5 kg was 2.76.

This paper assesses the extent of premature births and other adverse effects associated with maternal tobacco use during pregnancy in India.

## MATERIAL AND METHODS

In order to estimate the population impact of adverse reproductive outcomes due to maternal tobacco use in India, one must know the prevalence of tobacco use among women during pregnancy and the relative risk estimates. Relative risk estimates are available from the studies (4,7,8,12) described above. There has been no nationwide prevalence survey of tobacco use in India, but studies in some selected rural areas show that 10-62% of women use tobacco in one form or another (13,14). Overall, it has been estimated that at least 10% of women use smokeless tobacco, and an additional 2.5% smoke (15). Thus, it can be calculated that, in 1986, about 20.5 million women of reproductive age (15-44 years) were using tobacco in India.

## RESULTS

Table 1 shows the population attributable risks associated with tobacco use for stillbirth and birthweight of 2.5 kg or less in all babies

**Table 1**

*Estimated impact on reproductive outcome attributable to maternal tobacco use in India, 1986*

Reproductive outcome	Population attributable risk (%)		
	Odds ratio	Smokeless tobacco users	<i>Bidi</i> smokers
Stillbirth <sup>a</sup>	3	16.7	4.8
<2.5 kg birthweight <sup>b</sup> (both genders)	3	16.7	4.8
<2.5 kg birthweight <sup>b</sup> (girls)	7	37.5	13.0
<2.0 kg birthweight <sup>b</sup>	5.4	30.5	9.9
2-2.5 kg birthweight	2.8	15.3	4.3
Perinatal mortality <sup>c</sup>	2	9.0	2.4

<sup>a</sup>Source: ref. (7)

<sup>b</sup>Source: ref. (12)

<sup>c</sup>Source: ref. (4)

**Table 2**

*Estimated deaths from adverse reproductive outcomes due to tobacco use in pregnancy, India, 1986*

Reproductive outcome	Deaths ( $\times 10^3$ ) due to		
	Smokeless tobacco use	Smoking	Both
Stillbirth @ 25/1000 livebirths <sup>a</sup>	96	28	124
Prematurity-related deaths @ 41% <sup>b</sup>	151	43	194
Perinatal mortality @ 53/1000 livebirths <sup>c</sup>	110	29	139
Total	357	100	457

<sup>a</sup>Source: ref. (16)

<sup>b</sup>Source: ref. (17); figures for prevalence of premature births not available

<sup>c</sup>Source: ref. (17)



according to gender. Some 9% of perinatal mortality and nearly 17% of stillbirths could be attributed to tobacco use during pregnancy.

The estimated population load of such adverse reproductive outcomes is shown in Table 2. Overall, 457 000 deaths, of which 124 000 were stillbirths, 194 000 prematurity-related deaths, and 139 000 perinatal mortality, were estimated to have occurred in 1986 due to maternal tobacco use during pregnancy.

## DISCUSSION

Our analysis shows that nearly half a million deaths among infants and children aged less than five years might be due to maternal tobacco use during pregnancy. This is likely to

be an underestimate, since the risks for stillbirths were calculated on the basis of 25 stillbirths per 1000 in Bombay City (16) and stillbirths may be underreported, since all deliveries do not take place in hospital.

The higher death rates due to premature birth among female infants and children under the age of five may be due to the low birthweight of female babies, which in turn could be the outcome of maternal use of smokeless tobacco (12). As these relative risk estimates may change in the future with the availability of additional data, the present results must be viewed with caution. They nevertheless provide an estimate of the size of the problem and signal the need for action.

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# Influence of cigarette smoking and its cessation on the risk of cardiovascular disease

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Cigarette smoking contributes to the development of atherosclerotic lesions and to the clinical manifestations of coronary, aortic and peripheral vascular disease. A review of a 24-year prospective study among 17 000 US college alumni showed that excess risks for smokers over nonsmokers were 77% for total cardiovascular diseases, 98% for coronary heart disease, 52% for stroke, and 100% for other cardiovascular disease. A gradient increase in risks ranges steadily upward with increased smoking in a dose-dependent manner. Ex-smokers had a slightly higher risk than never-smokers. After adjusting for several factors, the relative risk for cardiovascular disease in alumni smokers over nonsmokers was 85%. Another review suggested that passive smoking carried a two-fold increased risk of fatal cardiovascular disease. There was a consistent gradient of reduction of risk for cardiovascular disease as the interval following smoking cessation increased. Cessation of cigarette smoking reduces the risk of these conditions, improves the quality of life and extends life expectancy.

## INTRODUCTION

It has been established unequivocally that cigarette smoking is a chief instigator of cardiovascular disease (CVD). In turn, fortunately, there is countering evidence that cessation of cigarette smoking leads to reduced incidence of CVD, hence implying potentially restored or increased longevity. Although the rates of cigarette smoking and CVD have declined in recent decades, both are still so widespread that remedial measures and intervention strategies are of prime interest. The present review was undertaken to evaluate the benefits of cessation of cigarette smoking, as compared with those of nonsmoking and in contrast to the hazards of continued smoking.

## METHODS

We identified studies of smoking and CVD reported from various nations in the past quarter century, which demonstrate that cigarette smoking contributes to the development of

atherosclerotic lesions and to clinical manifestations of coronary, cerebral, aortic and peripheral vascular disease. Next, we reviewed findings on smoking habits and other personal characteristics on the risk of CVD among Harvard College alumni. Further studies are summarized concerning the influences of kinds, intensities and duration of smoking, including passive smoking, use of filters, cessation of cigarette smoking and interrelationships of smoking with other influences on risk of CVD. These include results from a follow-up of San Francisco Bay area longshoremen, and findings on the effects of changes in cigarette smoking habits and other influences on CVD risk among University of Pennsylvania alumni.

The summary conclusions reached from this review are: (1) Cigarette smoking is a pervasive habit that increases the risks of both non-fatal and fatal CVD. (2) Cessation of



cigarette smoking reduces these risks, lowers the risk of premature death and thus may restore normal life expectancy. (3) Ex-smokers may retain higher risks than never-smokers. (4) Adverse effects of passive smoking appear to parallel those of active smoking, differing only in degree.

## RESULTS

**Representative world studies:** Among men in the Framingham (Massachusetts, USA) Heart Study in 1950-68, age-adjusted rates for total coronary heart disease (CHD) showed a gradient increase from nonsmokers to ex-smokers, to light smokers, to more than double for smokers of a pack or more of cigarettes per day (1,2). About 20% of the events were sudden deaths, which displayed a similar gradient. Heavy smokers had higher rates of coronary insufficiency, angina pectoris and myocardial infarction than nonsmokers. The parallel trends support a causal association between cigarette smoking and development of CHD.

Similar parallels found in other study populations corroborate the causal hypothesis (3-6). Among 290 000 US military veterans aged 35-84 years, whose smoking experience in 1917-40 coincided with an era of increased cigarette smoking and rising rates of CHD, the risk of fatal heart attack was 58% higher for smokers than for nonsmokers during a 16-year (1953-69) follow-up (7-9).

The American Cancer Society sponsored four-year studies of cigarette-smoking practices and exposure among 188 000 men aged 50-70 years in nine states, and 358 000 men and 483 000 women aged 35-84 years in 25 states (10-12). Of 20 116 deaths from CHD, more than 11 500 represented excesses attributable to smoking, or a 46% increased risk in men and 41% in women.

Of 3405 CHD deaths in six years among 78 000 Canadian veterans aged 30-90 years, there was a 60% excess among smokers as

compared to nonsmokers (13). A similar elevation of risk was found among 16 000 California men aged 35-64 years and engaged in nine occupations, with 1718 deaths from CHD in eight years (14).

The risk of dying from CHD for cigarette smokers exceeded that of nonsmokers by 60% among 34 000 men and by 100% among 6194 women who were British physicians followed-up for 20 and 22 years and had experienced 3191 and 179 CHD deaths, respectively (15,16).

In Sweden, random samples of 27 000 men and 28 000 women aged 35-64 years had 916 and 457 deaths from CHD in 10 years, indicating 70% and 30% higher risks of fatal CHD for smokers compared to nonsmokers, respectively (17).

In 29 health districts in Japan, 122 000 men and 143 000 women aged 40 or more were followed-up for 13 years; the 3351 and 2653 deaths from CHD showed that the excess risk for smokers over nonsmokers was 71% for men and 78% for women (18,19).

A study of 1212 deaths among 3749 Swiss physicians followed-up for 10 years indicated that mortality rates from CHD increased with number of cigarettes smoked per day, excess mortality being 33% for up to 10 cigarettes and 118% for 35 or more (20).

In the Finnish cohort of the 'seven countries study', 335 of 1520 men followed-up for 25 years died from CHD, and the relative risk for smoking 10 or more cigarettes daily *versus* never smoking was 1.95 (95% CI, 1.36-2.79) (21).

The consistency of these and many other massive global studies provides overwhelming evidence of the causative influence of cigarette smoking on CHD and on other CVD, including sudden death. Although understanding of the precise pathophysiological basis of these manifestations is incomplete, it appears that



**Table 1**

*Age-adjusted rates and relative risks of coronary heart disease (nonfatal and fatal) and cardiovascular disease (fatal) among 16 936 Harvard College alumni, by cigarette smoking habit*

Cigarette smoking (no. per day)	Prevalence (man-years, %)	No. of cases	Cases per 10 000 man-years	Relative risk of disease	<i>p</i> for trend
Coronary heart disease (nonfatal and fatal), 1962-72					
≥20	27	179	70.9	1.65	<0.0001
10-19	6	40	67.2	1.57	
1-9	7	38	53.4	1.25	
Former	36	178	39.0	0.91	
Never	24	90	42.9	1.00	
All cardiovascular disease (fatal), 1962-85					
≥20	27	385	57.5	2.27	<0.0001
10-19	6	59	35.1	1.39	
1-9	5	71	34.6	1.37	
Former	38	440	31.0	1.22	
Never	24	159	25.3	1.00	

cigarette smoking accelerates the atherosclerotic process by promoting myocardial oxygen insufficiency, lowers serum high-density lipoprotein levels, disrupts the haemostatic system, and lowers the threshold of ventricular fibrillation (2,22-26). The nicotine and carbon monoxide present in cigarette smoke are considered to be the most important agents, but hydrogen cyanide, oxides of nitrogen and carbon disulfide are also likely suspects in the pathogenesis of CHD (27). The patterns and mechanisms of invasion are so manifold that total avoidance of exposure to cigarette smoke is the only practical way of escaping its hazardous influences.

**Studies among US college alumni:** Data were obtained on 16 936 former students aged 35-74 years and initially free of CHD, who entered Harvard University in 1916-50. Recorded in student health archives and in mailed questionnaires returned by alumni in 1962 or 1966, these data were reviewed for personal characteristics, including the cigarette smoking, that might influence health. Follow-up data were obtained from repeat questionnaires in 1972 for non-fatal CHD and

from official death certificates through 1985 for both CHD and CVD. The overall experience represented by this study population spans the 20th century from 1900 to the present, as in 1985 the ages of surviving study subjects ranged from 52-92 years (28-30). During the follow-up of six to ten years (1966 or 1962 to 1972), there were 572 first attacks of CHD, 357 non-fatal and 215 fatal. When incidence rates were computed per 10 000 man-years, the overall risk for smokers was 68% higher than that for nonsmokers.

Mortality rates for fatal CVD were computed similarly for the 24-year follow-up from 1962 or 1966 through 1985, during which there were 1176 CVD deaths. Excess mortality risks for smokers over nonsmokers were 75% for CVD and CHD, 50% for stroke, and 100% for other CVD.

Table 1 shows age-adjusted rates and relative risks for total CHD and fatal CVD, for their respective follow-up intervals, by number of cigarettes smoked. Prevalence (as percentage of man-years) showed a distribution of about one-quarter heavy smokers, one-third



ex-smokers, and one-quarter never-smokers. The overall pattern of risk was similar for CHD and fatal CVD. As the number of ciga-

rettes smoked increased from none to a pack or more per day, the excess risk for CHD ranged upward to 65% and for CVD death to 127%.

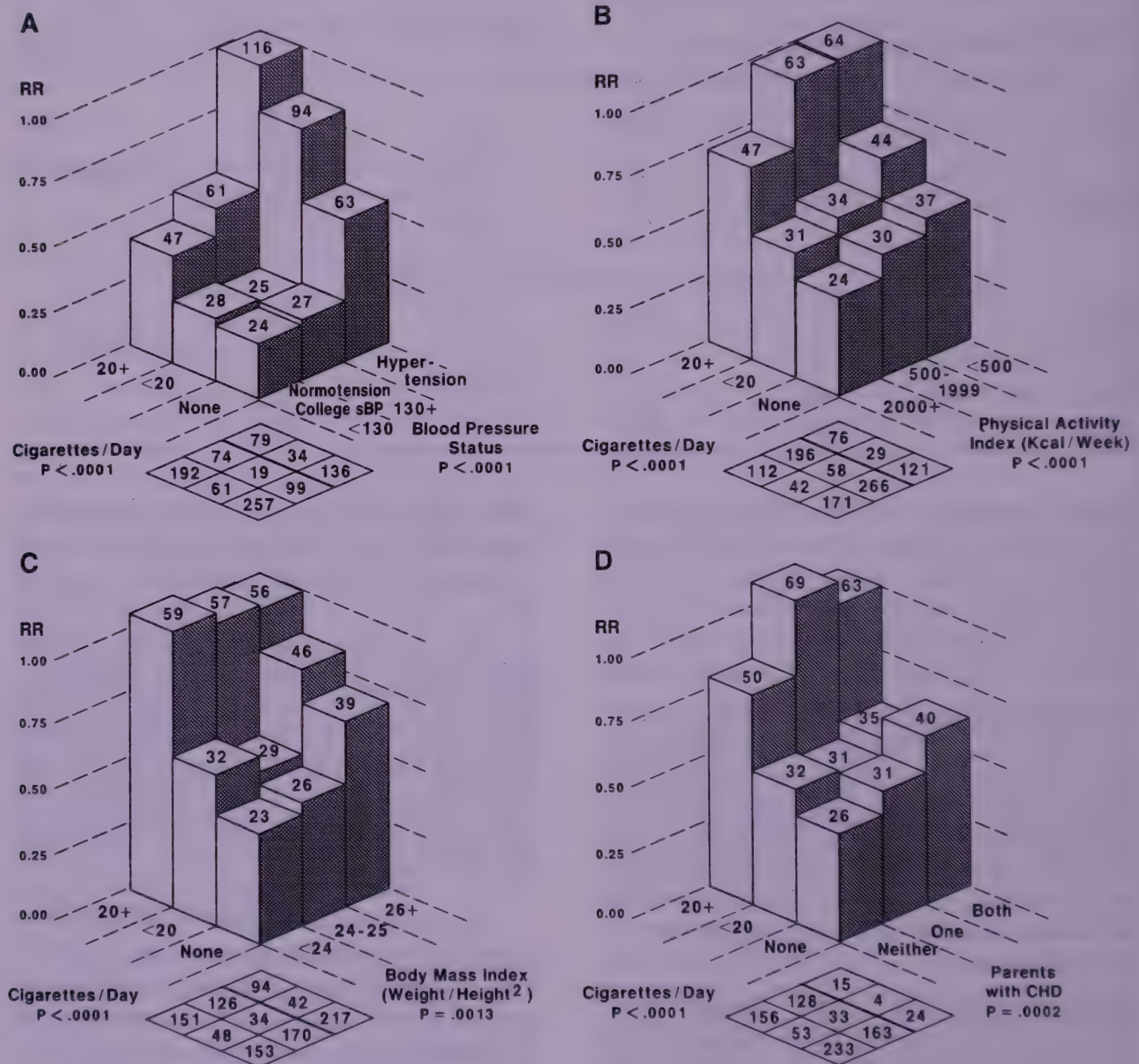


Fig. 1. Age-adjusted death rates of death from cardiovascular disease per 10 000 man-years of observation and relative risks among 16 936 Harvard College alumni, by cross-tabulations of cigarette smoking habit and

A. Blood pressure status

B. Physical activity index

C. Body mass index, and

D. History of parental coronary heart disease

Death rates are given on top of columns and corresponding numbers of deaths in the diamond-shaped keys. A RR of 1.00 is assigned to the paired combination with presumed highest risk (each back-corner column)



Figure 1 is a graphical presentation of cross-tabulations of cigarette smoking habit with other personal characteristics of the alumni: blood pressure status, physical activity, body-mass index (weight for height) (2) and parental history of CHD. Mortality rates from CVD are shown on top of the columns, and numbers of deaths are given in a corresponding grid beneath each graph. Column heights and their vertical scale show relative risks *versus* the presumed highest risk of 1.00 assigned to the back corner column in each figure. The other columns are located by breakpoints, chosen to provide three levels of each characteristic for comparisons. Column heights are comparable within each graph but not between graphs. Mortality trends may be seen as per the influence of each characteristic, holding constant the age and the paired characteristic. This permits recognition of any interacting influence of cigarette smoking with the other characteristic.

The three smoking levels represented in each graph are 'heavy' (20 or more cigarettes per day), 'moderate' (1-19 per day) and 'none' (ex-smoker or never-smoker), which contributed 26%, 12% and 62% man-years, respectively.

Blood pressure status categories identified normotensive alumni, whose systolic blood pressure as a student had been on record as either below 130 mm Hg or higher, and alumni with physician-diagnosed hypertension self-reported by questionnaire. Each category contributed 70%, 21% and 9% of the man-years of observation, respectively.

Physical activity categories were established by an index in estimated kilocalories per week, totalled from questionnaire-reported leisure-time walking, stair-climbing and sports play. The high-activity group expended 2000 kcal or more per week, moderately active men 500-1999, and sedentary men under 500 kcal per week; each group contributed 38%, 46% and 16% man-years, respectively.

Three weight-for-height groups defined by body mass index (BMI), computed as weight in kilograms divided by square of height in meters, were 'heavy' ( $\text{BMI} \geq 26$  units), 'medium-build' (24-25 units), and 'slender' ( $< 24$  units), who contributed 28%, 35% and 37% of man-years, respectively.

The three categories of alumni identified by parental history of CHD were those with both parents free of such illness, those with one parent afflicted and those with both parents having had CHD; each contributing were 64%, 34% and 3% of man-years, respectively.

In Figure 1A, the rates and relative risks for fatal CVD are cross-tabulated by cigarette smoking and blood pressure status. In all blood pressure categories, nonsmokers had half the risk of heavy smokers. The effect of cigarette smoking on the risk for fatal CVD was strong and independent of the influence of hypertension, which was even stronger.

At each level of cigarette smoking in Figure 1B, there is a decline in mortality from CVD as leisure-time physical activity increases. With adjustment for the influence of smoking, exercise continued to be related inversely to the risk for fatal CVD. Cigarette smoking was directly related to CVD mortality when exercise was held constant. The most physically active nonsmokers had only 38%, and the least physically active nonsmokers had 47%, as much fatal CVD as the sedentary heavy smokers.

Figure 1C shows that CVD mortality is related directly to the cigarette habit when BMI is held constant. With smoking held constant, CVD was related directly also to BMI, although less strongly than was smoking. The leanest nonsmokers (no more than 10% over 'ideal' weight, i.e., with BMI below 24 units) had only 42% as much risk as their heavy smoking, more obese classmates who used a pack or more of cigarettes per day and had a BMI score of 26 or higher.



Figure 1D presents cross-tabulated CVD risks for cigarette smoking and parental CHD. Insofar as parental CHD may imply a familial or hereditary tendency toward fatal CVD in alumni, the risk attached to that trend is much reduced for the nonsmoking alumni as compared with heavy smokers, being one-third lower even for nonsmokers with a double history of parental CHD, compared to the similar heavy smokers. The trend of lower CVD

mortality with reduction of cigarette smoking is substantial, and the influence of parental CHD status is nearly as strong. Here, as in all the other cross-tabulations, there is a consistent gradient lowering of fatal CVD risk as cigarette smoking is reduced from heavy to light to none.

Table 2 gives relative and attributable risks for total CHD in 10 years and of fatal CVD during 24 years of follow-up, by selected

**Table 2**

*Relative and attributable risks of coronary heart disease (nonfatal and fatal) and cardiovascular disease (fatal) among 16 936 Harvard College alumni, by selected adverse characteristics*

Characteristic	Prevalence (man-years, %)	Relative risk of disease			<i>p</i>	Attributable risk (%)	
		Age-adj.	Multi-adj.	95% CI <sup>a</sup>		Individual	Population
Coronary heart disease (nonfatal and fatal), 1962-72							
Cigarette smoking <sup>b</sup>	40	1.67	1.64	1.31-2.02	<0.0001	39	16
Hypertension <sup>c</sup>	9	2.26	2.00	1.55-2.58	<0.0001	50	5
Sedentary living <sup>d</sup>	63	1.51	1.34	1.06-1.69	0.0146	25	16
Overweight for height <sup>e</sup>	28	1.34	1.24	0.99-1.56	0.0555	20	6
History of parental CHD <sup>f</sup>	37	1.46	1.32	1.07-1.64	0.0100	24	9
One or more of above	89	2.54	2.53	1.48-4.33	0.0007 <sup>g</sup>	61	54
All cardiovascular disease (fatal), 1962-85							
Cigarette smoking <sup>b</sup>	39	1.70	1.84	1.59-2.14	<0.0001	46	18
Hypertension <sup>c</sup>	9	2.60	2.16	1.81-2.58	<0.0001	54	5
Sedentary living <sup>d</sup>	62	1.30	1.23	1.04-1.44	0.0130	19	12
Overweight for height <sup>e</sup>	28	1.33	1.36	1.16-1.59	0.0001	26	7
History of parental CHD <sup>f</sup>	37	1.22	1.14	0.98-1.32	0.0981	12	4
One or more of above	89	3.34	3.27	2.16-4.96	<0.0001 <sup>g</sup>	70	62

<sup>a</sup>Adjusted for differences in age and other characteristics listed

<sup>b</sup>Any amount

<sup>c</sup>Physician-diagnosed

<sup>d</sup>Expending less than 2000 kilocalories per week in walking, stair-climbing and recreational activities

<sup>e</sup>Body-mass index, 26+ (kg/m<sup>2</sup>), About 25% or more over ideal weight-for-height by 1959 Metropolitan Life Insurance Standards

<sup>f</sup>One or both parents with coronary heart disease

<sup>g</sup>Adjusted for differences in age only



characteristics known to predispose to these outcomes. The relative risk estimates are derived from a multivariate analysis (31) and computed for the presence *versus* the absence of each adverse characteristic, with adjustments for age and each of the other four characteristics listed. After allowing for each other variable, cigarette smokers had a 64% higher risk of fatal or non-fatal CHD than nonsmokers; hypertensive alumni had twice the risk of normotensives; sedentary men had 34% more risk than physically active men; obese men were 24% more at risk than slender men; alumni with a parental history of CHD had a 32% greater likelihood of developing CHD themselves than classmates without such family background; and men with any one or more of these adversities had two and one-half times the risk of CHD than their classmates with none of them.

The tabulated, individual attributable risks are estimates of the percent reduction in risk of CHD for persons who might have exchanged an adverse characteristic for its more healthful opposite. Reformed cigarette smokers might have had 39% less risk of developing CHD. Similarly, hypertensive men who achieved normal blood pressures might have halved their risk, and sedentary men who became more active might have reduced their CHD hazard by one-quarter. Overweight men might have had 20% lower risk if they gained less; men with a history of parental CHD might have experienced a 24% reduced risk if both parents had been free of CHD. If an alumnus with one or more of these adverse characteristics could have avoided all of them, his risk of heart attack during the follow-up might have been reduced by 61%.

Population attributable risk is an estimate of the potential reduction in the incidence of CHD in the Harvard alumni community if its unfavourable characteristics had been corrected to more healthful one. These estimates take the prevalence of the characteristic in the

population into account. As seen in Table 2, total abstinence from cigarettes by the alumni might have cut their CHD rate by 16%; abolition of hypertension by 5% (relatively small because of the low prevalence of hypertension); a universal physically active life style, 16%; elimination of obesity (about 25% over ideal weight for height), 6%; avoidance of CHD by parents, 9%; and elimination of all these adverse traits in the alumni population might have lowered the CHD experience by 54%.

Relative and attributable risks of mortality from CVD (bottom deck of Table 2) for these same five alumnus characteristics are of the same general magnitude as those given for CHD. There might have been 62% fewer CVD deaths during the interval 1962-85 if all five adversities had been absent.

Table 3 presents age-adjusted rates and relative risks for CHD by specific combinations of the three strongest predictors of increased CHD incidence: cigarette smoking, hypertension and sedentary living. Men with none of these characteristics experienced 26.2 attacks per 10 000 man-years; using this rate as base, relative risks in the presence of any one or any combination of characteristics ranged upward to 7.70 with all three characteristics combined. Presence of any one characteristic is accompanied by a 50% increase in risk, and in the presence of any two characteristics the risk is nearly tripled. The estimated percentage reductions that could have been anticipated over the 6- to 10-year follow-up, if alumni had avoided these adverse traits, were computed as population attributable risks. Elimination of the cigarette habit might have reduced CHD incidence by 25 ( $\text{SE} \pm 4$ )%; control of hypertension, 16 ( $\pm 2$ )%; avoidance of sedentary living, 26 ( $\pm 6$ )%; side-stepping any two characteristics, 31 ( $\pm 6$ )%; and by abolishing all three adverse characteristics, the alumni population might have spared themselves a hefty 48 ( $\pm 7$ )% of their risk for CHD during the follow-up period.



**Table 3**

*Age-adjusted rates and relative risks for coronary heart disease (nonfatal and fatal) among 16 936 Harvard College alumni, 1962-72, by specific combinations of adverse characteristics*

Cigarette smoking	Hypertension	Sedentary living <sup>a</sup>	Man-years of observation	Cases per 10 000 man-years	Relative risk of disease
+	+	+	1 712	201.9	7.70
+	-	+	18 319	65.5	2.78
-	+	+	2 618	102.3	
+	+	-	1 020	79.5	
-	-	+	26 684	35.1	1.50
+	-	-	11 809	50.1	
-	+	-	1 434	41.8	
-	-	-	18 648	26.2	

<sup>a</sup>Expending less than 2000 kcal per week in walking, stair-climbing and recreational activities

These observations fortify evidence advanced in other studies of leisure-time exercise (32-37) and of occupational physical activity (38-44), showing that avoidance of each of these personal characteristics has a protective influence against CHD. For example, the relative influence of heavy cigarette smoking, higher levels of blood pressure and strenuous cargo-handling by 3686 San Francisco Bay area longshoremen were assessed for the risk of death from CHD in a 22-year follow-up, 1951-72 (44). There were 395 deaths from fatal heart attack before age 75. Smoking a pack or more of cigarettes per day, a level representing 36% of the man-years contributed by these stevedores, increased the risk of fatal CHD by 109% over that of men smoking less or not at all. Systolic blood pressure equal to or greater than average (representing 42% of the man-years) led to a 106% increase. Nearly two-thirds of the workforce expended 8500 kcal or more per week in handling cargo at the quay, while the remaining men, who were warehousemen, supervisors, clerks and machine operators, expended less than 8500 kcal per

week. The less active group had a 97% higher risk of fatal CHD than the cargo-handlers. The risk estimates for each of these characteristics were adjusted for differences in age and both of the other characteristics.

Age-adjusted rates and relative risks of fatal CHD by specified combinations of heavy cigarette smoking, higher systolic blood pressure levels and low work-energy output are given for longshoremen in Table 4. Since relatively few longshoremen lacked all three characteristics, the basis for comparison was taken as the rate (40.3 per 10 000 man-years) of the presence of only one or none of the characteristics. From this basis, the risk for any two characteristics approximated an increase of 90%, and for all three characteristics, 280%. Thus if all longshoremen had smoked less than a pack of cigarettes per day or not at all, the death rate from CHD might have been reduced by 28 ( $\pm 4$ )%; if all systolic blood pressure levels had been less than the mean for five-year age groups, 29 ( $\pm 4$ )%; if all longshoremen had worked at high energy output levels, 49



**Table 4**

*Age-adjusted rates and relative risks of death from coronary heart disease among San Francisco Bay Area longshoremen, 1951-72, by specific combinations of adverse characteristics*

Cigarette smoking ≥1 pack/day	Systolic BP ≥ mean level	Low work-energy output <sup>a</sup>	Man-years of observation	Deaths per 10 000 man-years	Relative risk of death
+	+	+	5 493	151.9	22.68 3.77
+	-	+	9 595	71.3	78.3 10.65 1.94
-	+	+	10 072	75.2	
+	+	-	2 664	177.2	
-	-	+	14 087	55.9	8.35
+	-	-	3 705	25.4	40.3 3.80 1.00
-	+	-	4 687	68.1	
-	-	-	6 645	6.7	

<sup>a</sup>Expending fewer than 8500 kcal per week in job assignments

( $\pm 9$ )%; and if all three of these adverse characteristics had not existed, the corresponding total reduction in fatal CHD attacks might have approximated 88 ( $\pm 9$ )%. These computations are, of course, theoretical, in that they assume a causal relationship between each characteristic and fatal heart attack, that the characteristics are modifiable, and that other traits or conditions that influence the risk of fatal CHD are evenly divided between groups at high- and low-risk levels of these three characteristics. The percentage reductions would vary with strength of the relationship and with the proportion of the experience involving each characteristic. Yet, it is clear that removal of these hazardous life style elements might result in substantial reductions in the risk for fatal CHD.

It may be of some interest to compare and contrast the risk patterns of the Harvard alumni and San Francisco longshoremen, in view of their substantial differences in education, occupation, socioeconomic circumstances and other personal and environmental charac-

teristics. The relative risk for fatal CHD among the longshoremen was computed for cargo-handlers expending 8500-10 750 kcal per week and their less active fellows putting out 4750-8250 kcal, while the Harvard energy expenditure was split at only 2000 kcal per week. The assessments for longshoremen were based on measurements of actual oxygen consumption on the job, whereas the Harvard alumni estimates were derived from self-assessment of habitual activities, largely in leisure time. The assessments of longshoremen did not include spare time activities, which from questionnaire data were largely sedentary, and the alumni estimates did not include job activity requirements, which for executives in a 40-h work week approximate 4500-5500 kcal. Thus, the differences in energy output between stevedores and executives must be narrowed when occupational and recreational activities are considered jointly. Most importantly, both populations experienced lower CHD risk with higher levels of energy output. More active subjects had lower CHD risks within their own populations, and although



different cutpoints of blood pressure level and cigarette smoking habit were used, the hazardous effect of high levels of these two characteristics in each population is evident, as measured in both relative and attributable risks of CHD. In view of this finding, perhaps we may generalize to other populations or even be specific to an individual, concerning the hazards and benefits of these characteristics, especially cigarette smoking and its abandonment.

Another method of gauging the benefit of smoking cessation and removing the hazard of other adverse characteristics is by estimating the years of life to be gained by having the benefits of favourable life style characteristics, including abstinence from cigarette smoking. Actuarial models provide estimates of added years of life to be gained up to age 80, as derived from Harvard alumni mortality experiences. Results are given in Table 5 for five-year age groups at the start of follow-up and for three characteristics, namely cigarette

smoking, blood pressure status and physical activity. The estimated number of years gained from practising each favourable pattern of a characteristic is adjusted for differences in the other two patterns. The bottom line of the table provides weighted average gains in life expectancy for each favourable characteristic, from age 35 to age 80, with adjustments for differences in age and each of the other two patterns. The data suggest that the largest gain (2.7 years) would be achieved by avoiding hypertension, the next largest gain by not smoking cigarettes (2.3 years), and the third by being physically active<sup>c</sup> sufficiently to expend 2000 kcal or more per week in leisure pursuits (1.2 years). Ways of living that would combine all of these favourable characteristics might be expected to gain further added life, since their influences are partly independent. Eschewing of cigarette smoking might reduce the risk of death from CHD, stroke, aneurysm, chronic obstructive lung disease and lung and other cancers, thus providing a substantial benefit. Functional capacity maintained by

**Table 5**

*Added years of life from favourable characteristics<sup>a</sup> in men up to the age of 80 years, as estimated from Harvard College alumni mortality experiences, 1962-78*

Age at entry (years)	Cigarette abstinence <i>versus</i> cigarette smoking <sup>b</sup>	Normotension <i>versus</i> hypertension <sup>c</sup>	Active life style <i>versus</i> sedentary living <sup>d</sup>
35-39	2.68	3.48	1.50
40-44	2.62	3.31	1.39
45-49	2.38	2.60	1.10
50-54	2.23	2.20	1.20
55-59	2.00	1.84	1.13
60-64	1.64	1.51	0.93
65-69	0.98	1.20	0.67
70-74	0.51	0.37	0.44
75-79	0.03	0.18	0.30
35-79 <sup>e</sup>	2.26	2.72	1.25

<sup>a</sup>Each pattern of characteristics is adjusted for differences in the other patterns listed

<sup>b</sup>Any amount

<sup>c</sup>Physician-diagnosed

<sup>d</sup>Expending less than 2000 kcal per week in walking, stair-climbing and recreational activities

<sup>e</sup>Weighted average adjusted for differences in age and the other patterns listed



adequate exercise would tend to promote longevity by reducing the risk of CHD and of the hypertension that predisposes to CHD by perhaps other mechanisms.

**Cessation of cigarette smoking:** In several of the global studies summarized earlier, the influence of cessation of cigarette smoking on the risk for CHD among men was examined by interval since quitting, age at cessation and intensity and duration of cigarette use. Risk declined in a gradient for ex-smokers as their interval since quitting cigarettes increased. The pattern was seen for both heavy and light smokers of all ages, although it was less impressive beyond age 65. After 10 years, they had little or no more risk than never-smokers. As mentioned earlier, these were massive studies involving thousands of study subjects and up to 20 years of follow-up, so the data on ex-smokers may have become fairly well-stabilized. Those referred to here were groups of British physicians (15,16), US men surveyed by the American Cancer Society in 25 states (11,12) and a Swedish random sample (17).

Recent retrospective observations of 910 women aged 25-64 at the time of first myocardial infarction, and of 2375 hospital-based control subjects, indicated that the relative risk for this disease among smokers, as compared with never-smokers, was 3.6 (95% confidence interval, 3.0-4.4) (45). Women who had stopped smoking less than two years previously still had a sizeable added risk (2.6; 1.8-3.8); however, the relative risk fell promptly thereafter, and the risk among women who had not smoked for three or more years was virtually indistinguishable from that among women who reported never to have smoked. The patterns of decline following smoking cessation were similar regardless of the amount smoked, the duration of smoking, the age of former smokers or the presence or absence of such other predictors of increased risk of myocardial infarction as hypertension, higher levels of blood cholesterol and history of angina pectoris. Thus, the data for these women suggested

that the increase in risk for first non-fatal myocardial infarction from cigarette smoking declined sharply within a year or so of quitting, and it nearly disappeared after three years of smoking cessation.

Since a large-scale, randomized clinical trial is unlikely ever to become practicable, the most persuasive evidence that smoking cessation and other life style improvements can reduce CVD death rates is to be found in cohort studies such as that illustrated in Table 6, where 6242 University of Pennsylvania alumni were identified as smokers, ex-smokers and never-smokers and followed for subsequent CVD. In 1962, these men were asked about their smoking habits; about 40% smoked and 60% did not. In 1976, the same men were questioned again. The table shows that 18% had continued to smoke, 21% had quit smoking and the 60% who had not smoked were still nonsmokers. (Nonsmokers in 1962 who took up smoking by 1976 were too few to tabulate or analyse). Next, these three cohorts — smokers, ex-smokers and never-smokers — were followed-up to 1985 for CVD. By 1985, they were 62-80 years old, and 223 had died of CVD in the 60 193 man-years of observation; however, the ex-smokers, those who quit cigarette smoking between 1962 and 1976, had a 50% less risk of dying from CVD than those of their classmates who had kept on smoking. The never-smokers continued to enjoy the lowest risk of all — 57% less than that of the smokers, but the ex-smokers had nearly equalled that score with a risk far below their former high-risk status as smokers.

Studies of this kind may be termed 'natural history' experiments, in which we examine what is going on in real life, and the findings obtained are convincing testimony that any personal or community programme of cigarette smoking cessation that takes root successfully will be worthwhile in terms of reduced risk for CVD. Of course, since cigarette smoking is also responsible for many other illnesses, such as cancers and chronic obstructive lung



Table 6

*Age-adjusted rates and relative risks of death from cardiovascular disease among 6242 University of Pennsylvania alumni, 1976-85, by changes in selected characteristics between 1962 and 1976*

Characteristic	Year		Prevalence (man-years, %)	No. of deaths	Deaths per 10 000 man-years	Relative risk of death
	1962	1976				
Cigarette smoking <sup>a</sup>	Yes	Yes	18	72	67.9	1.00
	Yes	No	21	43	33.6	0.50
	No	No	60	105	29.4	0.43
Hypertension status <sup>b</sup>	Yes	Yes	7	36	82.6	1.00
	No	Yes	15	44	47.3	0.57
	No	No	78	143	30.7	0.37
Vigorous physical activity <sup>c</sup>	No	No	50	136	44.3	1.00
	Yes	No	15	36	37.5	0.85
	No	Yes	14	19	24.0	0.54
	Yes	Yes	21	30	26.7	0.60

<sup>a</sup>Any amount

<sup>b</sup>Physician diagnosed

<sup>c</sup>Activities of sufficient intensity and duration to work up a sweat, and likely to require expenditure of  $\geq 7.5$  kcal/min.

disease, the benefits of the same intervention programme will be more extensive than shown in Table 6. Moreover, the table shows that the University of Pennsylvania alumni were subject to further hazards and benefits associated with other prominent influences on CVD risk, i.e., blood pressure status and physical activity level. The cross-tabulations in Figure 1 have already shown that there are important interrelationships between these and the impact of cigarette smoking. Benefits of non-smoking and ample exercise accrue at all levels of these characteristics shown by various studies (46,47). It is safe to assume that the conclusions on smoking and health reached from studying Harvard College alumni are valid for University of Pennsylvania alumni, and *vice versa*. Indeed, the most important findings, those which can be used to formulate policies and programmes to discourage smoking and promote good health, are applicable to all the populations, as the global reports we have reviewed imply. Those US college alumni who improved their life style and quit smoking

cigarettes have enjoyed lifelong benefits not only for themselves but demonstrated them to everyone else. They are being joined by many others everywhere, and perhaps this is the major reason the incidence of CHD and CVD has been falling in recent decades.

**Intervention studies:** The Framingham Heart Study undertook to assess whether the use of filter cigarettes conferred a smaller risk of CHD than non-filter cigarettes. No such benefit was found in 14 years of follow-up (48).

Despite widespread public information programmes on the hazards of cigarette smoking, the results of specific intervention projects have been slow, spotty and disappointing, according to some reports (49). Still, there has been some noticeable progress. One of the most influential movements against cigarette smoking was based chiefly on the hazards of passive smoking, even though research findings on this environmental assault appeared at first to be somewhat inconclusive (50-53). Recently, in Washington County (Maryland,



USA), over a 12-year period, the relative risk for fatal CHD among passive smoking men was found to be 1.31 (1.05-1.64), as compared with unexposed men; the corresponding risk among women was 1.19 (1.04-1.36) (54). During a four-year follow-up of 7997 men and women in western Scotland, the relative risk for mortality from CHD was 2.01 (1.21-3.35) for passive smokers as compared with control subjects (55). Smoking in public places, such as restaurants, theatres, aircraft, subways, transport vehicles and hotel rooms, has become progressively more restricted or even banned outright (56).

A study of smoking trends in Wisconsin was based on annual *per-caput* sales of cigarettes during the years 1950-88, and these data were derived from records of excise taxes imposed at distribution centres (57). The results showed that cigarette shipments dropped sharply in the 1980s after taxes

were increased and smoking regulations were imposed by law. The development of restrictions on public smoking tends to reduce individual opportunities to light up, leading apparently to a drop in actual cigarette consumption and sales. The socially hostile influence of a nonsmoking environment also seems to present a strong incentive for cigarette smoking to go out of style. Even in many private homes, as in doctors' offices and elsewhere, neat little signs have become common that read, 'Thank you for not smoking'.

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# Tobacco smoking, exposure to environmental tobacco smoke and respiratory disease

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The association between cigarette smoking and chronic obstructive airway diseases is well established. There is adequate evidence linking exposure to environmental tobacco smoke, or passive smoking, with respiratory disease and impairment of lung function, especially among children. Smoking and exposure to environmental tobacco smoke worsen bronchial asthma. In a study of morbidity indices and lung function in three groups of asthmatics — nonsmokers, nonsmokers exposed to environmental tobacco smoke and smokers, each group comprising 50 patients — showed significant differences.

## INTRODUCTION

Tobacco smoking plays a vital role in the causation of respiratory disorders. The role of smoking as a risk factor for chronic obstructive airway diseases has been well reviewed (1,2). This paper gives an overview on this subject and presents the findings from a study of the effect of smoking in asthmatics.

## CHRONIC OBSTRUCTIVE AIRWAY DISEASES IN INDIA

The prevalence of chronic bronchitis is high among Indian smokers (3,4). In Bombay, cough, dyspnoea or both was observed among 39% of smokers and 13% of nonsmokers (5), and studies in North India revealed a high prevalence of chronic bronchitis and obstructive airway diseases (6,7). In urban Chandigarh and rural Mullapur in North India, chronic bronchitis was diagnosed in 9.9% and 16.4% of male smokers and in only 0.9% and 4.1% of nonsmokers (6). In a study in Shimla, Himachal Pradesh, 32% of male and 52% of female *bidi* smokers had chronic obstructive airway disease. Among reverse *chutta* smokers

in Orissa, in areas adjoining Andhra Pradesh, 33% of the sample had this condition (8).

## SMOKING AND AIRWAY OBSTRUCTION

Regular cigarette smoking increases phlegm production and airway obstruction (9), and in susceptible smokers airway obstruction is often irreversible (10). The effect of smoking on reversible airway obstruction in asthmatics is under investigation. The response to treatment for asthma is poorer among smokers than nonsmokers (11). A steep fall in the forced expiratory volume was shown among smokers with bronchoreactivity (12).

## EXPOSURE TO ENVIRONMENTAL TOBACCO SMOKE

Studies in western countries have shown that exposure to environmental tobacco smoke (ETS), or passive smoking, also known as secondary or involuntary smoking, is associated with impaired lung function, increased rates of respiratory illness and chronic airway disease (13-15). In asthmatic children, exposure to



ETS leads to increased severity of the disease (16).

### A STUDY ON 150 INDIANS WITH BRONCHIAL ASTHMA

**Objective:** The objective of this investigation was to assess the effects of active smoking and of exposure to ETS on the treatment of bronchial asthma.

**Material and methods:** 150 male asthmatic patients aged 15-50 years were selected. The diagnostic criteria for asthma consisted of a history of at least one wheezing episode in the preceding year, followed by a demonstration of reversible airway obstruction as observed by at least 20% improvement of forced expiratory volume in 1 second (FEV<sub>1</sub>) after salbutamol inhalation. Patients with a history of hospitalization, an acute attack of asthma or parenteral drug administration in the preceding two weeks were not included in the study. At the time of the investigation, the clinical condition of the patients was stable, requiring no more than two daily maintenance doses of bronchodilators.

The clinical status of the disease was assessed for the preceding year from the number of visits made by the patients to their physician, their history of hospitalization, if any, number of acute asthmatic episodes, history of parenteral drug administration related to the asthmatic condition and corticosteroid

intake. The amount and duration of maintenance drugs was also recorded.

The patient's history with regard to smoking and/or exposure to ETS was registered with the help of a questionnaire. The smoking status of the patients was assessed on an objective scale which included the type of smoking, frequency and its duration.

Exposure to ETS was defined as the presence of at least one regular smoker among the close entourage of the patient, either at home or at work, for at least one year preceding the onset of illness. Exposure to ETS could thus have been from a parent, spouse or sibling at home or from sharing the same table or a room at college or at the office with a smoker.

The patients were grouped into three categories: group 1 consisted of nonsmokers with no exposure to ETS; group 2 were nonsmokers with exposure to ETS; and group 3 were smokers. Fifty patients were accumulated in each group, giving a total of 150. The mean ages of the patients in the three groups were comparable, namely, 35.8, 35.4 and 35.1 years, respectively. The mean durations of exposure to ETS (group 2) and of smoking (group 3) were  $20.1 \pm 4.8$  years and  $18.5 \pm 4.7$  years, respectively.

Lung function was assessed using standard techniques, measuring expiratory flow rates by spirometry. The values observed were expressed as a percentage of the predicted normal values derived in this laboratory (17).

**Table 1**

*Mean age and spirometric function ( $\pm$ SD) of asthmatics*

Group	Age	Spirometric function (% predicted)			
		FVC	FEV <sub>1</sub>	FEV <sub>1</sub> /FVC	FEF <sub>25-75%</sub>
Nonsmokers	35.8 $\pm$ 6.1	72.1 $\pm$ 6.4	74.2 $\pm$ 5.7	72.2 $\pm$ 6.7	73.2 $\pm$ 8.8
Nonsmokers exposed to ETS	35.4 $\pm$ 5.2	59.8 $\pm$ 5.2*	60.2 $\pm$ 6.4*	60.1 $\pm$ 7.8*	64.3 $\pm$ 9.5*
Smokers	35.1 $\pm$ 5.8	53.1 $\pm$ 6.4*	53.1 $\pm$ 6.6*	55.2 $\pm$ 4.8*	58.4 $\pm$ 8.6*

ETS, environmental tobacco smoke

\*Significantly lower than nonsmokers ( $p < 0.05$ )



**Table 2**  
*Morbidity indices in asthmatics*

Morbidity index	Nonsmokers		Nonsmokers exposed to ETS		Smokers	
	Mean	%	Mean	%	Mean	%
No. of acute attacks	5	10	8*	16	8*	16
Hospital admission						
No. of patients	4	8	8*	16	9*	18
Total no. of admissions <sup>a</sup>	8	16	16*	32	20*	40
Mean duration (days)	4.5		5.5		6.2	
Requiring parenteral drugs (no. of patients)	11	22	18*	36	18*	36
Requiring maintenance drugs (no. of patients)						
Continuous	18	36	28*	56	37*	74
Intermittent	32	64	22	44	13	26
Steroids	8	16	12*	24	14*	28

ETS, environmental tobacco smoke

\*Significantly different from nonsmokers ( $p < 0.05$ )

<sup>a</sup>More than one admission required for the same patient

**Results:** The spirometric indices revealed significantly greater airway obstruction in groups 2 and 3 (Table 1).

More patients in group 2 had required hospital admissions, steroids, parenteral drug administration and maintenance bronchodilators than in group 1. Acute asthmatic attacks were more frequent in groups 2 and 3 than in group 1 (Table 2).

**Discussion:** This study shows that smoking and exposure to ETS have adverse effects on the treatment of asthmatic patients. The worsening of airway obstruction is due to the reflex stimulation of parasympathetic pathways by the smoke particles. Asthmatics, characterized as such by increased airway responsiveness to various stimuli, react abnormally to particulate matter (18). Even in nonasthmatic patients, cigarette and *bidi* smoking are known to increase bronchial responsiveness (19-22).

Exposure to ETS may also increase airway responsiveness, as demonstrated earlier (23). For instance, there were significantly more hyperresponders among nonsmoking, nonatopic, healthy wives of smokers than of nonsmokers. This hyperresponsiveness in active and passive smokers is likely to be worse in asthmatics, who are already hyper-responsive.

Although there were no children in this study, it is pertinent to point out that parental smoking exacerbates respiratory diseases in children: data from western countries show that the occurrence of cough and cold and the risk of hospitalization for respiratory illness among children increased when one or both parents were smokers (24). Furthermore, asthmatic children of mothers who smoked had lower expiratory flow rates and more emergency room visits than those with nonsmoking mothers (16,25). These observations emphasize the consequences for children of exposure to ETS.



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# **EXPERIMENTAL AND DIAGNOSTIC ASPECTS**





# Advances in tobacco carcinogenesis: I. Smokeless tobacco and betel quid

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Although consumption of loose-leaf, plug and twist tobacco has decreased since 1984 in the USA and elsewhere, the consumption of oral snuff continues to rise in the USA and in Scandinavia. Epidemiological data indicate that oral use of snuff and chewing of betel quid with tobacco are carcinogenic to humans. Smokeless tobacco contains several known carcinogens, including volatile aldehydes, *N*-nitrosamines, lactones, benzo[*a*]pyrene, nickel, cadmium, the radioactive polonium-210 and uranium, nitrosamino acids and, as major carcinogens, tobacco-specific *N*-nitrosamines. The latter occur at exceptionally high levels in snuff, exceeding the suggested upper limit for nitrosamines in other consumer products by three orders of magnitude. Betel quid with tobacco contains not only the tobacco-specific carcinogens but also genotoxic agents derived from the areca-nut alkaloid, arecoline. In recent years, snuff has been shown to be carcinogenic in the oral cavity of rats. Other types of smokeless tobacco and betel quid with and without tobacco also induce tumours in laboratory animals; however, the reported rates were statistically insignificant. The biomarkers developed for measuring the intake of smokeless tobacco constituents by chewers and snuff dippers are haemoglobin adducts formed with metabolites of tobacco-specific nitrosamines in the blood of smokeless tobacco users. It is possible to reduce the carcinogens in chewing and snuff tobaccos.

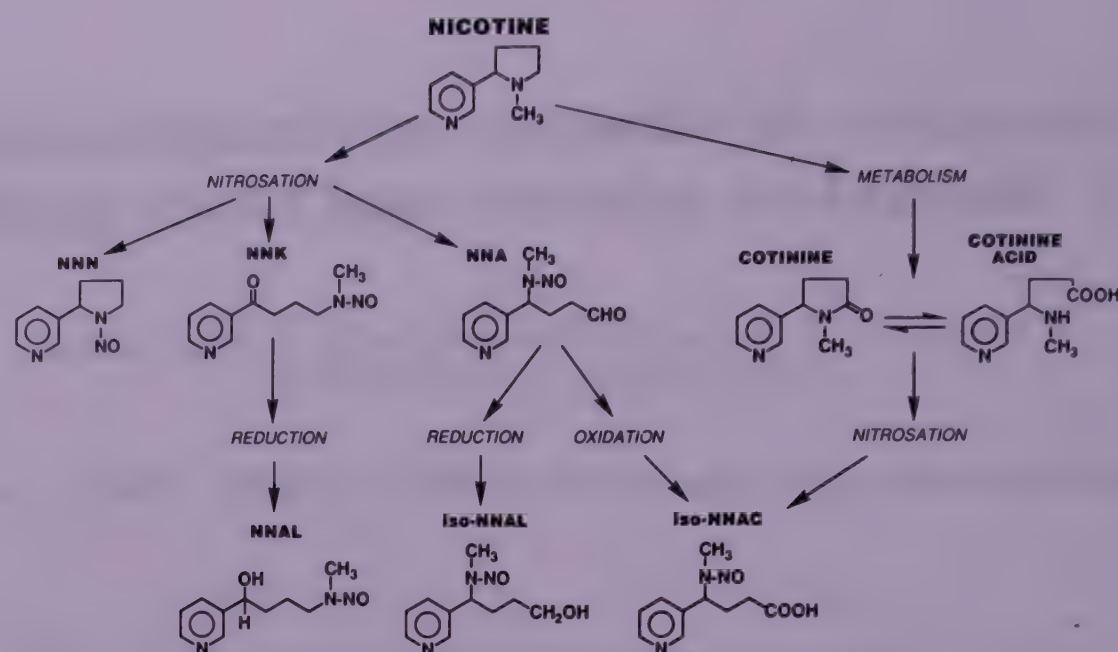
## INTRODUCTION

In 1984, the carcinogenicity of chewing tobacco, oral snuff, nasal snuff and betel quid was critically evaluated by a working group of the International Agency for Research on Cancer (1) and, in 1986, by an Advisory Committee to the Surgeon-General of the US Public Health Service (2). Both panels concluded that snuff dipping is carcinogenic in humans and that chewing of tobacco alone is most likely also carcinogenic in humans. The available evidence was inadequate for an evaluation of the carcinogenicity of chewing tobacco and of snuff in laboratory animals. The IARC Working Group concluded also that there exists 'sufficient' evidence for the

carcinogenicity in humans of betel quid that contains tobacco. The data for evaluation of the carcinogenicity of betel quid in animals were regarded as 'inadequate' (1).

Four types of smokeless tobacco are marketed in developed countries. These are loose-leaf tobacco, plug tobacco, twist tobacco and snuff. The latter type is manufactured in the form of dry and moist snuff and is intended for nasal and oral use (1,3). In this overview we will not discuss orally used smokeless tobacco products such as *khaini*, *kiwam*, *masheri* (syn. *mishri*), *nass* and *naswar* (1,3), primarily because of the paucity of data. The fact that these products are consumed daily by millions of people in Asia and elsewhere is a compelling



Fig. 1. *N*-Nitrosation of nicotine

reason to gather more research data on their health effects and to develop preventive strategies.

Between 1961 and 1984, the production of smokeless tobacco in the USA increased by about 36%, i.e., by 61 000 metric tonnes. Since then, production has significantly decreased (by 23%), and this trend continues. Unfortunately, during the last four-year period, the manufacture of moist snuff has increased by 7%, i.e., by 1820 metric tonnes (2-4). Since snuff is apparently the most carcinogenic form of smokeless tobacco (1,5) and is increasingly being used by adolescents (6), both educational efforts and research need to be intensified in order to reduce the risk for disease and primarily that for oral cancer (7).

In this paper we will review the recent studies on the carcinogenicity of smokeless tobacco and betel quid with emphasis on the chemistry, bioassays, biochemistry and chemoprevention of the carcinogenic effects of orally-used tobacco products.

## CARCINOGENIC AGENTS IN SMOKELESS TOBACCO

Natural tobacco contains at least 3050 different compounds (8). Furthermore, smokeless

tobacco may be enhanced by flavouring agents, added in the form of plant extracts and/or as chemicals (8-10). Among 23 tumorigenic agents thus far isolated and identified (Tables 1 and 2) in smokeless tobacco (11-21) are volatile aldehydes and *N*-nitrosamines, *N*-nitrosamino acids, lactones, polynuclear aromatic hydrocarbons, certain metals and the  $\alpha$ -emitters, polonium-210 and uranium-235 and -238. The most abundant strong carcinogenic compounds in smokeless tobacco are the tobacco-specific *N*-nitrosamines (TSNA). These are formed by *N*-nitrosation of the major habituating tobacco alkaloid, nicotine, and of minor *Nicotiana* alkaloids during tobacco harvesting, curing, fermentation and ageing. Seven TSNA have been identified (Fig. 1) in smokeless tobacco (14,22). Of these, *N*'-nitrososornicotine (NNN) and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) are the predominant carcinogens in smokeless tobaccos. In a risk assessment in 1981, the National Research Council estimated exposures of US residents to nitrosamines (23): a nonsmoker is exposed to about 1.0  $\mu\text{g/day}$  of carcinogenic nitrosamines; a smoker of 20 cigarettes is exposed to about 11.4  $\mu\text{g/day}$ . On the basis of the average values for the two leading US snuff brands in



**Table 1**  
*Carcinogenic agents in smokeless tobacco*

Carcinogen	Smokeless tobacco <sup>a</sup>	Concentration (ng/g)	Ref. no.
<b>Volatile aldehydes</b>			
Formaldehyde	NT, S	2200 - 7400	11,12
Acetaldehyde	NT, S	1400 - 27 400	11,12
Crotonaldehyde	S	200 - 2400	12
<b>Volatile N-nitrosamines</b>			
Nitrosodimethylamine	CT, S	ND - 220	2,12
Nitrosopyrrolidine	CT, S	ND - 337	2,12
Nitrosopiperidine	CT, S	ND - 107	2
Nitrosomorpholine	CT, S	ND - 690	2,12
Nitrosodiethanolamine	CT, S	40 - 6800	12
<b>N-Nitrosamino acids</b>			
Nitrososarcosine	S	present	2
3-(Methylnitrosamino)-propionic acid	CT, S	200 - 7400	13,14
4-(Methylnitrosamino)-butyric acid	CT, S	ND - 1770	13,14
<b>Tobacco-specific N-nitrosamines</b>			
N <sup>2</sup> -Nitrosonornicotine	CT, S	400 - 154 000	2,12,13,15
4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone	CT, S	ND - 13 600	2,12,13,15
4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanol	S	present	2
N <sup>2</sup> -Nitrosoanabasine	CT, S	present - 560	2,12
<b>Lactones</b>			
α-Angelica lactone	NT	present	17
β-Angelica lactone	NT	present	17
Coumarine	NT	600	18
<b>Polynuclear aromatic hydrocarbons</b>			
Benzo[a]pyrene	NT, S	>0.1 - 90	11,12
<b>Metals</b>			
Nickel	NT,ST,S	180 - 2700	11,19,20
Cadmium	ST	700 - 790	19
Polonium-210	NT, S	0.3 - 0.64 pCi/g	11,12
Uranium-235 and -238	S	2.4 - 19.1 pCi/g	11,21

<sup>a</sup>CT, chewing tobacco; NT, natural tobacco; S, snuff  
ND, not detected

1986, a dipper consuming 10 g of snuff per day (24) is exposed to about 278 µg of carcinogenic nitrosamines (Table 2) (12). Analyses of the saliva of tobacco chewers and snuff dippers have clearly demonstrated that the carcinogenic TSNA are extracted during chewing (16,25-28). TSNA metabolites were shown to bind to haemoglobin in the blood of snuff dippers (29). In addition to the TSNA extracted

from chewing tobacco, the body burden of TSNA also probably derives from endogenous nitrosation of the alkaloids during chewing and snuff dipping (29,30).

We are academically in agreement with the evaluation criteria for carcinogenic agents set by the International Agency for Research on Cancer, which consider NNN and NNK as 'possible carcinogens to humans' (31);

however, we place greater emphasis on the harmful effects of excessive concentrations of these highly carcinogenic TSNA in smokeless tobacco and in the saliva of snuff dippers. These high levels of *N*-nitrosamines in smokeless tobacco would not be tolerated in any other consumer product. For example, in the USA, permissible upper limits of nitrosamines in bacon and beer have been set at 5 ng/g by Federal regulations (32,33).

### BIOASSAYS WITH SMOKELESS TOBACCO

Upon systemic administration, nicotine induces morphological alterations in the microvasculature of the oral mucosa of rats (34). This effect may contribute to the development of lesions in the mucosa of rats upon treatment

of the oral cavity with smokeless tobacco or extracts thereof (1,2,35). This nicotine effect also probably enhances the occurrence of early changes in the oral mucosa of Syrian golden hamsters in which snuff was inserted in their pouches (1,2,36).

In 1981, Hirsch and Johansson reported on a method which enables repeated exposure of the oral mucosa of rats to snuff and to saliva extracts of snuff. Twice-daily insertion of about 50 mg of snuff into a surgically created canal in the lower lip (37) has thus led to the induction of benign and malignant tumours of the oral cavity, liver and lung in rats (38-40). Chemical analyses of the saliva of the snuff-treated rats revealed the presence of nicotine and TSNA. These findings support the concept that the induction of tumours with smokeless tobacco

**Table 2**

*Estimated exposure of US residents to carcinogenic nitrosamines<sup>a</sup>*

Mode of exposure	Nitrosamines <sup>b</sup>	Primary exposure route	Daily intake ( $\mu$ g/person)
Beer	NDMA	Ingestion	0.34
Cosmetics	NDELA	Dermal absorption	0.41
Cured meat:			
Cooked bacon	NPYR	Ingestion	0.17
Scotch whiskey	NDMA	Ingestion	0.03
Cigarette smoking	VNA	Inhalation	0.3
	NDELA	Inhalation	0.5
	NNN	Inhalation	6.1
	NNK	Inhalation	2.9
	NAB	Inhalation	0.7
Snuff dipping <sup>c</sup>	VNA	Ingestion	0.45
	NDELA	Ingestion	3.2
	NNN	Ingestion	242.0
	NNK	Ingestion	12.3
	NAB	Ingestion	19.0

<sup>a</sup>From the National Research Council (23) amended by data for snuff dipping (12)

<sup>b</sup>Volatile *N*-nitrosamines (VNA), *N*-nitrosodimethylamine (NDMA); *N*-nitrosoethylmethylamine (NEMA); *N*-nitrosodiethylamine (NDEA); and *N*-nitrosopyrrolidine (NPYR)

<sup>c</sup>From Hoffmann *et al.* (12), average values for the two leading snuff brands which accounted in 1986 for about 90% of all moist snuff consumed in the USA (10 g/snuff/day)



requires repeated, extended exposure of the oral cavity to the tobacco carcinogens, which reflects the mode of exposure practised by oral tobacco users. However, snuff apparently also contains tumour inhibitors, which reduce or suppress the carcinogenic effect of a mixture of NNN and NNK (39). This inhibiting effect was observed by comparing results from long-term swabbing of the oral cavity of rats with snuff extract to those seen with a swabbing of a solution containing only 0.011% NNN and 0.0022% NNK (39). It is likely that the tumour inhibitors in smokeless tobacco diminish the enzymatic activation of the TSNA to their active forms, since a lower rate of DNA alkylation is seen after application of snuff extract. The observed tumour inhibiting effect is not caused by the nicotine in the tobacco (41).

Rats infected with herpes simplex virus type 1 (HSV-1) and treated by snuff insertions into the lip canal developed a higher rate of malignant oral tumours than groups of rats treated with either snuff or HSV-1 alone (42). In a group of Syrian golden hamsters inoculated with HSV-1 or HSV-2 and treated with snuff twice daily, 50% of the animals developed squamous-cell carcinomas of the buccal pouches after only six months; hamsters inoculated with HSV-1 or HSV-2 alone, or with snuff alone, did not develop oral tumours after six months (43). HSV is ubiquitous in humans and may be important as a cocarcinogen with NNN and NNK. Nevertheless, benign and malignant tumours have been induced in the oral cavity of rats by snuff without HSV infection, thus supporting the epidemiological findings (1,2).

## BETEL QUID

In most cases, betel quid contains areca nut, betel leaf, catechu and lime and is mixed with tobacco. The major constituents of areca nut are carbohydrates (47-85%), tannins (11-26%), protein (4.9-8.3%) and areca-specific alkaloids (0.15-0.67%) (1). The major

alkaloid is arecoline; and there are several minor alkaloids, namely arecaine, guvacine, guvacoline and arecolidine. Not only tobacco carcinogens (Table 1) but also several arecoline-derived genotoxic agents have been identified in betel quid. One of these, 3-(methylnitrosamino)-propionitrile (MNPN), is a strong carcinogen that is formed by *N*-nitrosation of arecoline. This reaction also yields 3-(methylnitrosamino) propionaldehyde (MNPA), *N*-nitrosoguvacoline (NG) and *N*-nitrosoguvacine (NGC) (Fig. 2) (43). MNPN induces benign and malignant tumours of the oesophagus, tongue, nasal cavity and liver of rats (43,44). It alkylates DNA *in vitro* and *in vivo* to 7-methylguanine, *O*<sup>6</sup>-methylguanine, 7-(2-cyanoethyl) guanine and *O*<sup>6</sup>-(2-cyanoethyl)guanine (Fig. 3) (45). MNPA is highly genotoxic (46); NG induces tumours of the exocrine pancreas in rats (47). NGC has not been bioassayed thus far.

Nair *et al.* (48) reported in 1985 the identification of two synthetic nitro musks which are apparently added to tobacco in betel quids and to perfumed tobaccos such as those used for chewing in India. These are musk ambrette

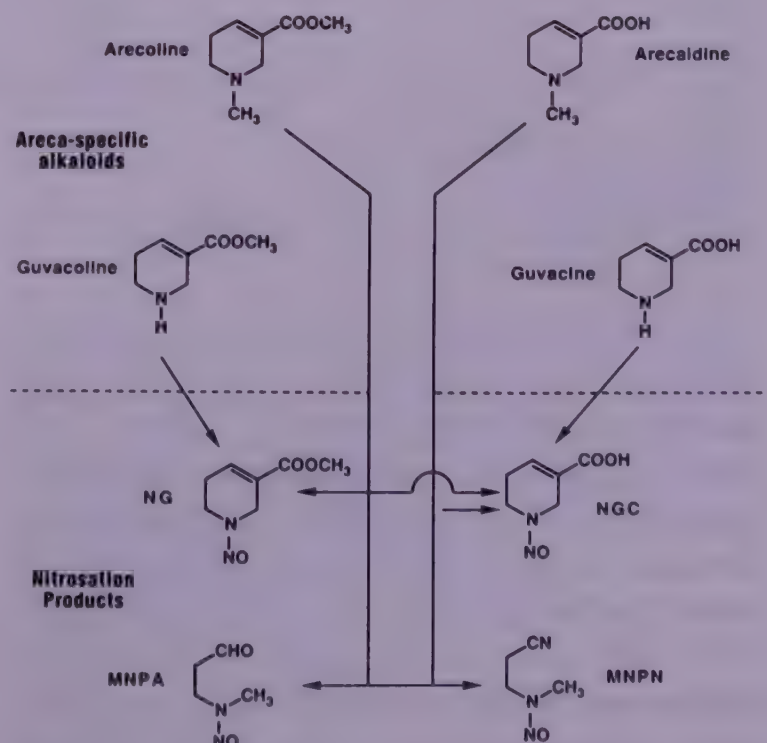


Fig. 2. Nitrosation products of *Areca*-alkaloids

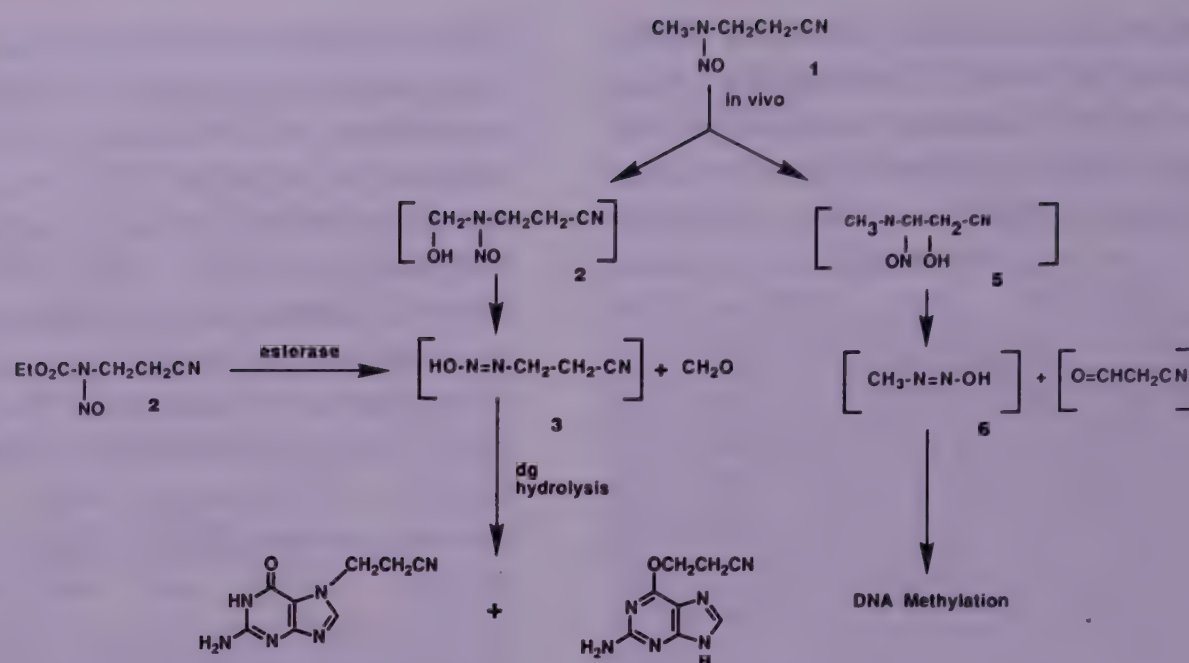
Fig. 3. Intermediates involved in the  $\alpha$ -hydroxylation of MNPN

Table 3

*Synthetic nitro musks in samples of betel quid with tobacco and perfumed chewing tobacco<sup>a</sup>*

Sample	mg/wet weight		Structure	
	Musk ambrette	Musk xylene	Musk ambrette	Musk xylene
BQT.1	1.10	0.60		
BQT.2	1.08	0.45		
BQT.3	0.92	0.49		
BQT.4	1.44	0.79		
BQT.5	0.82	0.47		
Z.1	23.5	ND		
Z.2	11.2	0.60		

<sup>a</sup>Modified from Nair *et al.* (48)

ND, not detected

BQT, betel quid with tobacco; Z, Zarda

(5-*t*-butyl-1,3-dinitro-4-methoxy-2-methylbenzene) and musk xylene (1-*t*-butyl-3,5-dimethyl-2,4,6-trinitrobenzene) (Table 3). Musk ambrette is genotoxic in *Salmonella typhimurium* TA100 (48). Betel quid made with tobacco also contains tumour inhibitors, of which hydroxychavicol has so far been identified (49). Yet, on the basis of our present knowledge, NNN and NNK seem to be the major carcinogens in betel quid-tobacco mixtures.

Betel quid with and without tobacco, and extracts thereof, induce some tumours of the skin and forestomach in mice and elicit tumours of the oral cavity in mice and hamsters (1). The rate of induction of oral tumours in laboratory animals with these materials was statistically not significant; nevertheless, the data are biologically important since the spontaneous rates of tumours of the oral cavity in mice and rats are very low, or practically non-existent (50,51).



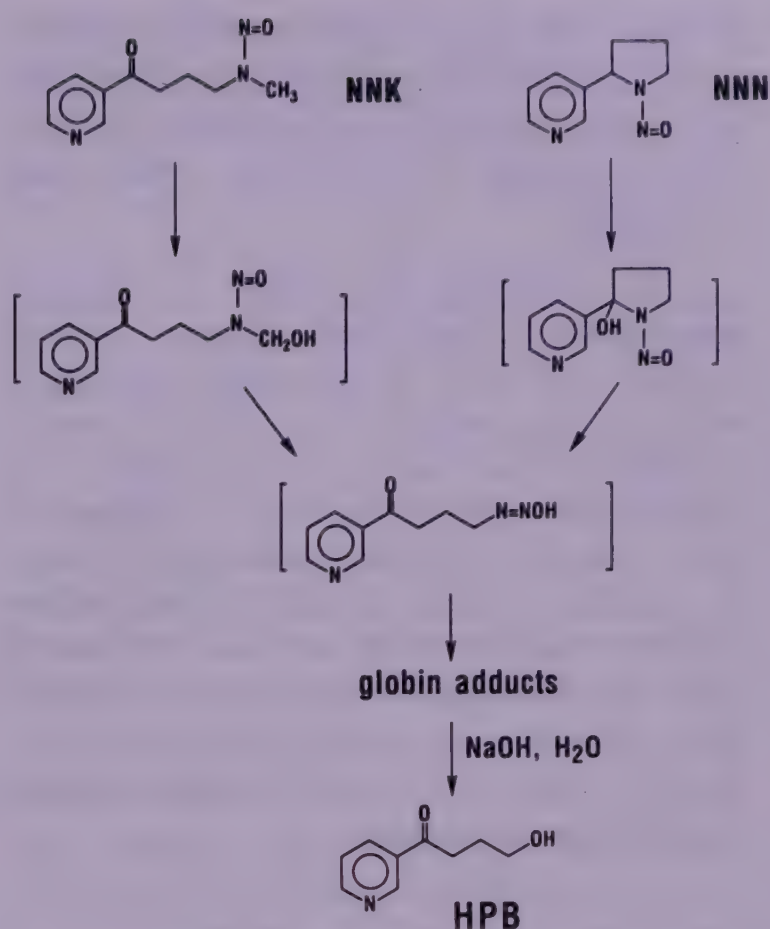
## BIOMARKERS

The intake of agents from smokeless tobacco by chewers and snuff dippers has been assayed by determining nicotine and its metabolite, cotinine, in saliva, serum and/or urine. These determinations involve gas chromatography or radioimmunoassays (52). Generally, the intensity and frequency of tobacco chewing is reflected in the levels of nicotine/cotinine found in physiological fluids. In snuff dippers, the reported cotinine concentration per ml saliva varied from 178 to 2480 ng; urine concentrations of cotinine were measured in the range of 14 to 4140 ng/mg creatinine, while urinary nicotine levels ranged from 17-3410 ng/mg creatinine (27).

In 1987, the utility as a marker of another major nicotine metabolite, namely *trans*-3'-hydroxycotinine, was reported. However, procedures using this marker of nicotine uptake have thus far been applied only to the analysis of urine of smokers and not for dosimetry in smokeless tobacco users (53).

A more recent validation test for the frequency and intensity of smokeless tobacco use has been based on the determination of strontium by X-ray fluorescence spectrometry in cells scraped from the oral mucosa of chewers or snuff dippers (54). Although this method has not been widely applied, it appears promising for assessment of recent exposure of the oral cavity to smokeless tobacco ( $\leq 2$  days).

The methods discussed above do not yield information about the intake of carcinogenic agents, unless the results are extrapolated. To obtain a more direct evaluation of exposure to carcinogens, Carmella *et al.* (29) developed a method that provides for measurement of globin adducts of NNN and NNK in the circulating blood of smokeless tobacco users. This method is based on the metabolic conversion of TSNA to a highly reactive electrophile, diazohydroxide (Fig. 4), which reacts with haemoglobin. The analysis requires 10 ml of blood. Mild base treatment of haemoglobin



**Fig. 4.** Metabolic activation of NNK and NNN to intermediates which bind to globin and release HPB in hydrolysates of human haemoglobin

adducted to NNK and/or NNN releases 4-hydroxy-1-butanone (HPB) (Fig. 4). HPB is enriched by solvent partitioning and is derivatized to its pentafluorobenzoate. After purification by high-performance liquid chromatography, the HPB derivative is analysed by capillary gas chromatography and detected by negative-ion chemical ionization mass spectrometry. Analysis of the blood of 22 snuff dippers revealed  $517 \pm 538$  fmol HPB/g haemoglobin; that of 21 nonusers showed the presence of  $29.3 \pm 25.9$  fmol HPB/g haemoglobin. This first result reflects the levels of exposure to the carcinogenic NNN and NNK derived from oral snuff, in addition to the NNN and NNK that is formed endogenously. In-depth analyses are needed to determine the levels of haemoglobin adducts formed with NNN and NNK as a function of chewing frequency and intensity.



Results will also probably reflect differences in metabolic rates of individual snuff dippers and/or the extent of inhibition of metabolic activation of TSNA by other snuff constituents.

To determine the intake of areca-nut components by betel-quid chewers, we have recently developed an analytical method in which a metabolite of arecoline, *N*-acetyl-cysteine-arecoline adduct, is quantified in the urine as the dimethylester (Fig. 5). The first 12 urine samples from betel-quid-tobacco chewers contained 12-92 ng/ml *N*-acetylcysteine-arecoline and 0.7-5.7 ng cotinine. We plan to apply this biomarker to specimens from a large group of betel-quid chewers in order to estimate the intake of arecoline from the betel quid under various conditions.

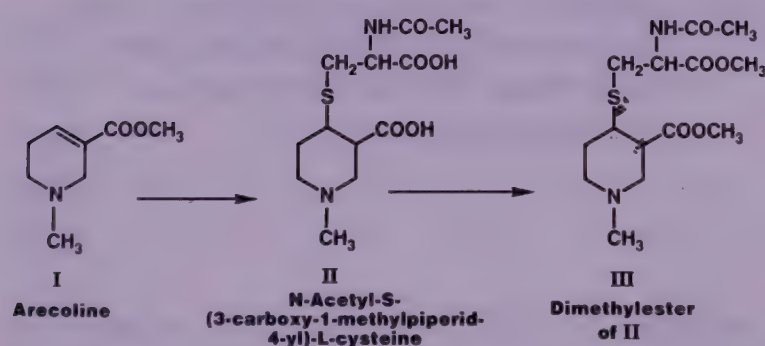


Fig. 5. Analysis of arecoline metabolite II in human urine

## REDUCTION OF THE CARCINOGENIC POTENTIAL OF SMOKELESS TOBACCO

We regard primary prevention of the usage of smokeless tobacco and betel quid to be highly important for reducing the risk for cancer, and especially the risk for oral cancer. The large-scale intervention studies in India through health education and programmes aimed at cessation of betel quid usage appear most promising (55) and deserve full support by health authorities (see paper by Gupta *et al.*, this volume). Chemopreventive approaches towards reducing the risk for cancer in chewers

of tobacco and betel quid have also been developed by various groups. For example, Stich and associates (56) found that supplementing the food of chewers of betel quid in Kerala, India, with  $\beta$ -carotene and vitamin A significantly reduced the frequency of micronucleated buccal mucosal cells, led to remission of oral leukoplakia and inhibited the development of new leukoplakias. It remains to be seen how far these chemopreventive measures will lead to a reduction in the incidence of oral cancer.

A third approach towards reducing the carcinogenic effects of smokeless tobacco is seen in product modification. The volatile, highly carcinogenic *N*-nitrosomorpholine (NMOR) is gradually disappearing from US snuff because this product is now sold in plastic boxes rather than in waxed cardboard containers, which were the major source of morpholine, the precursor of NMOR (57). Between 1981 and 1987, the concentration of NMOR in US snuff decreased from levels up to 690 ng/g to below the detection limit ( $\leq 2$  ng/g) in five of eight brands and to levels of 9-39 ng/g in three brands (12,57). *N*-nitrosodiethanolamine (NDELA) has also drastically decreased in smokeless tobaccos because its precursor, the maleic hydrazide-diethanol preparation MH-30 is no longer being used as a sucker control agent on tobacco plants. The diethanolamine gives rise to the carcinogenic NDELA during tobacco processing. In 1980, we measured up to 6840 ng NDELA/g in smokeless tobacco (58); the levels in present-day US products have decreased to 600 ng/g tobacco. The radioactive trace metals, polonium-210, uranium-235 and uranium-238 can be significantly reduced in tobacco by ascertaining that fertilizers are free of radioelements (59). Approaches towards the reduction of other carcinogens in smokeless tobacco have not been developed; however, reduction of the carcinogens other than TSNA and *N*-nitrosamino acids (NAC) in Table 1 may not be of major biological consequence.



TSNA and *N*-nitrosamino acids are the major classes of carcinogens in smokeless tobacco and in betel quid-tobacco mixtures. Most are formed after the harvesting of tobacco, during curing, fermentation and ageing. The major precursor of TSNA is nitrate, which is reduced to nitrite, the nitrosating agent for the tobacco alkaloids. For example, the nitrate-rich burley ribs yield significantly greater amounts of TSNA than do the laminae of the burley leaves (60,61); thus, eliminating burley ribs from chewing tobacco will result in lower levels of TSNA in the consumer product. The same result can also be achieved by drastically lowering the nitrate content of the ribs, by extraction or by bacterial degradation of nitrate, which leads to reduced forms of nitrogen. The higher the alkaloid concentration in the leaf, the higher is the concentration of TSNA in smokeless tobaccos (62). Thus, a reduction of nicotine and of the minor alkaloids will effectively lower the TSNA levels in the consumer product. Alkaloid levels in tobacco can be reduced by supercritical extrac-

tion with carbon dioxide (63). Curing and storage of tobacco also have a substantial influence on TSNA yields; higher temperatures (20°C) and higher humidity dramatically increase formation of these compounds (64,65). The cited examples underline the possibilities for changes in the preparation of smokeless tobacco products that could lead to reduced carcinogenic potential.

Although there is a lack of experimental data on reduction of *N*-nitrosamino acids, one can assume that a reduction of the nitrate content of the tobacco will also inhibit the formation of these compounds in smokeless tobacco.

### Acknowledgments

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# Advances in tobacco carcinogenesis:

## II. Cigarette smoke

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Since the first US Surgeon General's Report on Smoking and Health in 1964, studies have demonstrated that whole smoke and smoke particulates, though not the gas phase of cigarette smoke, elicit carcinogenic responses in mice, rats and hamsters. About 4000 chemical compounds have been identified in tobacco smoke; approximately 45 of these are known to be carcinogenic. The most abundant and strong carcinogens are the tobacco-specific *N*-nitrosamines (TSNA). These are formed from nicotine and the minor tobacco alkaloids during tobacco processing, smoking and most likely also endogenously upon smoke inhalation. Being pro-carcinogens, the TSNA require metabolic activation to form species that react with cellular macromolecules such as DNA and proteins. This activation occurs primarily by alpha-hydroxylation. Some of the DNA adducts are promutagens, i.e., they activate *K-ras* oncogenes. The latter have been isolated from the lungs of mice treated with TSNA. Adducts of TSNA with haemoglobin are employed in the dosimetry of exposure to tobacco carcinogens. Continued laboratory studies are essential to monitor new tobacco products, to develop methods for reducing the toxic and carcinogenic potential of tobacco smoke, and to gain a better understanding of the facts involved in the toxicity and carcinogenicity of tobacco smoke.

### INTRODUCTION

Epidemiological studies have demonstrated a causal association between cigarette smoking and cancer of the lung, upper aerodigestive tract, pancreas, renal pelvis and urinary bladder. Cigarette smoking has also been associated with cancer of the liver and uterine cervix, and with leukaemia (1-3). On the basis of these convincing epidemiological data, and considering the widespread awareness of smoking as a cause of cancer, one may ask why there is a need for further studies in tobacco carcinogenesis. While the scientific community endorses the goal of a 'smoke-free society' by the year 2000, recent statistics on cigarette consumption are not supportive of this goal. According to a World Health Organization report issued in 1986, a decrease in cigarette consumption *per caput* has been noted only in Europe, and

major increases in cigarette consumption have occurred in Africa, Latin America and Asia (4).

This review aims to document progress made in tobacco carcinogenesis during the last 25 years. Five aspects of the research in this field underscore the need for continued studies in tobacco carcinogenesis. These are: (i) the need for a better understanding of the mechanism of tobacco carcinogenesis, (ii) continued development of concepts for cigarettes with reduced smoke toxicity, (iii) monitoring of new tobacco products for toxicity and other biological activity, (iv) exploration of means for reducing the biological effects of cigarette smoke, and (v) establishment of biomarkers for measuring exposure of individuals to tobacco carcinogens and their metabolically activated forms. Inherent in these research endeavours is



our aim to contribute also to a better understanding of the mode of action of chemical carcinogens *per se*.

## CIGARETTE SMOKE

The freshly generated mainstream smoke (MS) of cigarettes is a highly dense aerosol with about  $10^{10}$  particles per milliliter. These lung-damaging particles range in diameter from 0.1 to 0.5  $\mu\text{m}$ , with a mean of 0.25  $\mu\text{m}$  (5). The pH of the smoke of cigarettes made of flue-cured (bright) tobacco, such as those sold in the United Kingdom, and of cigarettes made with tobacco blends, such as those sold in the USA, Japan, and most European countries, is weakly acidic; i.e., it lies between 5.5 and 6.2. The smoke of cigarettes made with burley or black tobaccos, such as those made in France, Cuba, parts of Italy, North Africa and South America, is weakly alkaline, with pH levels of 6.8-7.5. In the weakly acidic smoke, nicotine is protonated and occurs mainly in the particulate phase, while nicotine in the weakly alkaline smoke occurs in the more toxic, unprotonated form and is also present in the vapour phase (6).

About 95% by weight of the mainstream smoke emitted from a non-filter cigarette is comprised of 400-500 individual gaseous components, with nitrogen, oxygen and carbon dioxide constituting 85-92% of the total smoke. The particulate matter contains about 3500 different compounds, with nicotine as the most abundant single compound, amounting to 0.1-2.0 mg per cigarette (7,8). So far, about 45 carcinogens have been identified in cigarette smoke. They include 12 polynuclear aromatic hydrocarbons (PAH) with benzo[*a*]pyrene (BaP) as the major representative of this class; they also include aza-arenes, aromatic amines, such as the human bladder carcinogens 2-naphthylamine and 4-aminobiphenyl, and the lung carcinogen polonium-210. The gas phase contains such carcinogens as volatile *N*-nitrosamines, formaldehyde and other aldehydes, benzene, acrylo-

nitrile and vinyl chloride (Fig. 1) (8). The most abundant, strong carcinogens in cigarette smoke are the tobacco-specific *N*-nitrosamines (TSNA). These are formed by *N*-nitrosation of nicotine and minor tobacco alkaloids during tobacco processing, ageing and smoking (Fig. 2) (9).

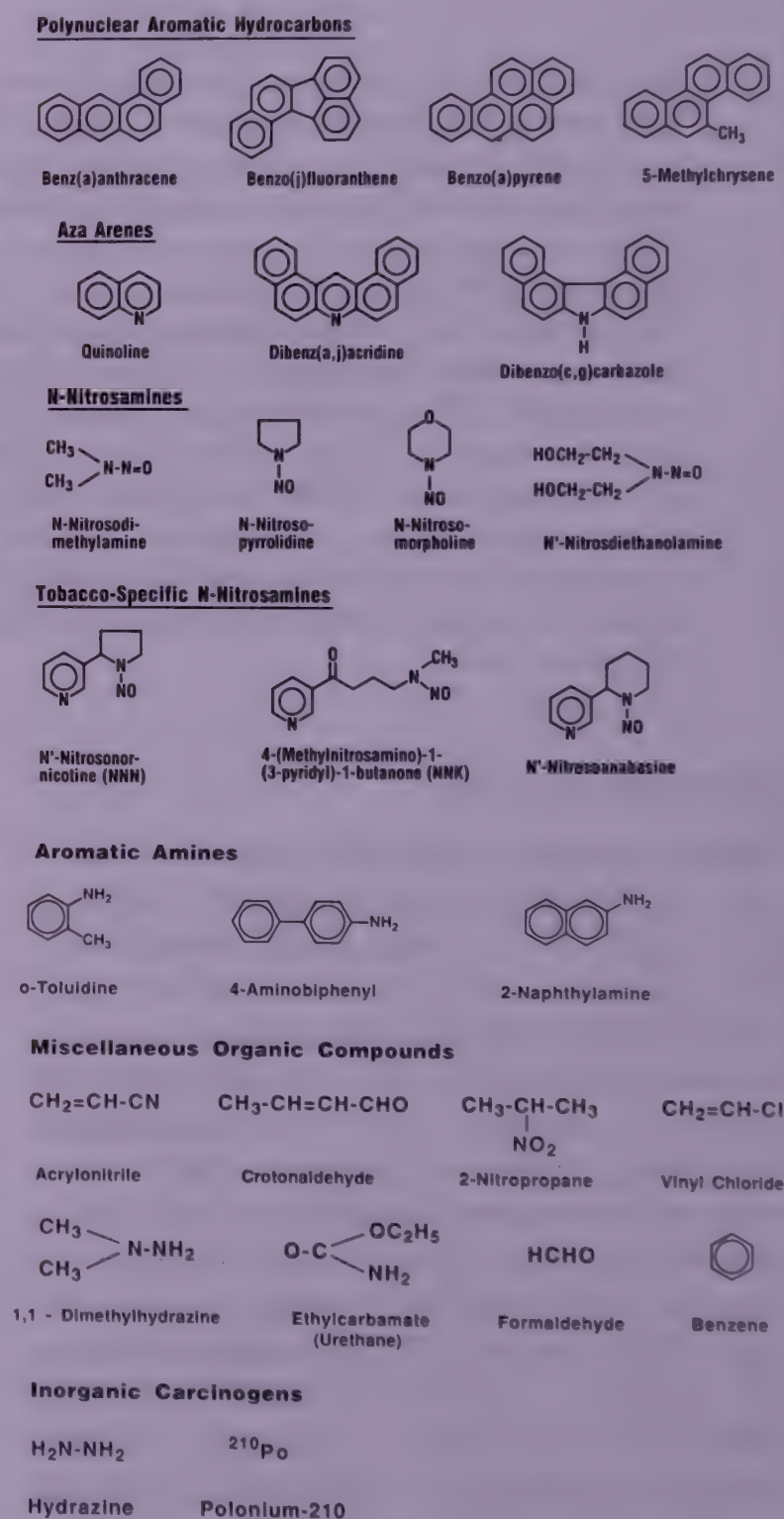


Fig. 1. Chemical structures of major tobacco smoke carcinogens



### FORMATION OF TOBACCO-SPECIFIC N-NITROSAMINES (TSNA)

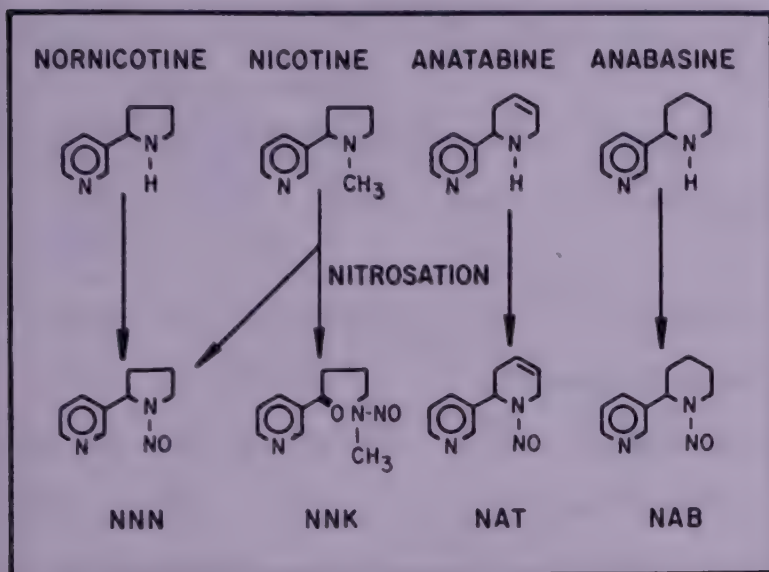


Fig. 2. N-nitrosation of tobacco alkaloids

### CIGARETTE SMOKE CARCINOGENS

**PAH:** Inhalation assays with mice, rats and hamsters have shown that the particulate matter of cigarette smoke induces malignant tumours of the respiratory tract (1,10,11). The particulate matter, tar, is more carcinogenic than the gas phase. Fractions and subfractions of the particulate matter have been assayed on the skin of mice and rabbits, and these show clearly that the greatest tumorigenic potential lies in those fractions that contain highly concentrated PAH (12). Yet, the PAH by themselves cannot account for the tumorigenic activity observed after treating the skin of mice and rabbits with the particulate matter. Fractionation studies and mouse skin assays have demonstrated that most of the tumorigenic potential of the particulate matter can be accounted for when the PAH-enriched

subfraction is tested together with the non-carcinogenic, weakly acidic fraction, which acts as a cocarcinogen (13). The major known cocarcinogenic agents in the weakly acidic fraction are the catechols (14).

It is well-recognized that PAH are carcinogenic at the site of application; thus, they can induce tumours in the respiratory tract of animals (11,15,16). The neutral subfraction of cigarette tar, in which the PAH are highly enriched, is the only fraction that induces squamous-cell tumours in the lung of rats upon intratracheal instillation (17). Biochemical studies lend further support to this evidence. Carcinogenic PAH are enzymatically activated to electrophiles that form covalently bound PAH-DNA adducts. BaP is activated *via* 7,8-dihydroxy-7,8-dihydro-BaP to its ultimate carcinogenic form, 7,8-dihydroxy-9,10-epoxy 7,8,9,10-tetrahydro-BaP (BPDE), which binds to DNA. Studies with rats, mice, hamsters and dogs have shown that BPDE binds to the DNA of cells in tracheobronchial tissues, and BPDE adducts with guanine and adenine have been isolated from animal tissues (Fig. 3). Similar BPDE-DNA adducts have been isolated from cultured explants of human tracheobronchial tissues that had been treated with BaP (18,19).

The degree of PAH exposure resulting from cigarette smoking makes it likely that these agents are causative etiological factors in cancers of the lung and upper respiratory tract. Repeated intratracheal instillation of BaP on ferric oxide at total doses of 15-45 mg/kg induced significant, dose-related percentages of tumours in the respiratory tract (20). Over

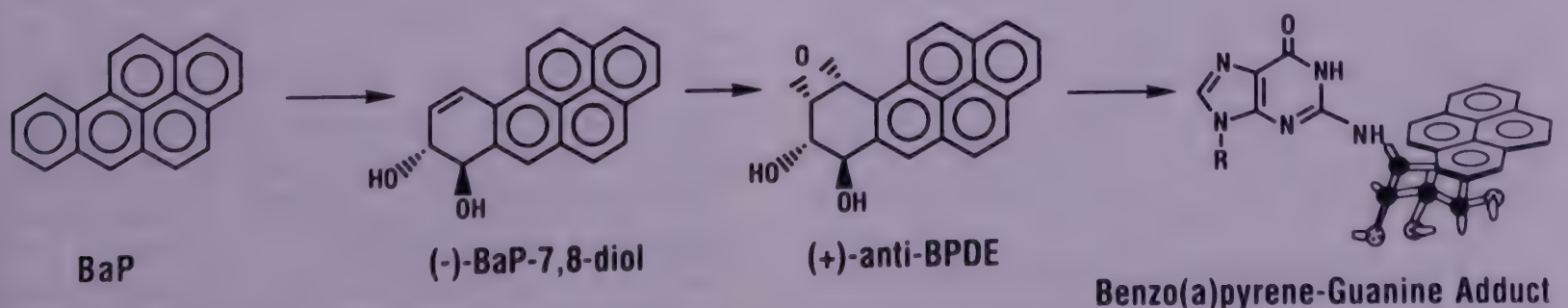


Fig. 3. Metabolic activation and DNA binding of benzo[a]pyrene



a 40-year period, a smoker of 40 non-filter cigarettes per day is exposed to approximately 20 mg BaP (about 0.3 mg/kg). Considering that this cumulative exposure affects primarily the respiratory tract of the smoker, the calculation for the whole body (per kg) dose is a conservative estimate of the exposure of the target tissues. Moreover, in addition to BaP, cigarette smoke contains 10 or more other carcinogenic PAH. Such reasoning brings us closer to the understanding that PAH do, in fact, play a significant role in the induction of cancer in the respiratory tract of cigarette smokers.

**Tobacco-specific N-nitrosamines (TSNA):** The most abundant, strong carcinogens in cigarette smoke are the TSNA. They are predominantly formed from nicotine, which is responsible for habituation to tobacco, and they are also formed from minor *Nicotiana* alkaloids (Fig. 2). TSNA concentrations in smoke are decisively influenced by the levels of nitrate in tobacco. Cigarettes with a high nitrate content, such as those made entirely of burley or black tobacco and those containing high amounts of ribs and stems of burley tobacco, deliver high levels of TSNA in the smoke (Table 1) (21-25). Of the seven TSNA identified to date, *N*-nitrosonornicotine (NNN) and 4-(methyl-nitrosamino)-1-(3-pyridyl)-1-butanone (NNK) are the most powerful carcinogens. NNK induces benign and malignant tumours of the lung, nasal cavity, pancreas and liver in rats, as well as tumours of the lung, trachea and nasal cavity in Syrian golden hamsters and lung tumours in mice. NNN elicits tumours of the oesophagus and nasal cavity in rats, tumours of the trachea and nasal cavity in Syrian golden hamsters and lung tumours in mice (26,27). Cultured explants of human tracheobronchial tissue treated with NNK, form basal-cell hyperplasia and squamous-cell metaplasia, comparable to the early changes seen in the bronchial epithelium of smokers (28).

The procarcinogenic TSNA, which are metabolically activated by  $\alpha$ -hydroxylation, form unstable  $\alpha$ -hydroxynitrosamines. These

**Table 1**  
*Tobacco-specific N-nitrosamines in mainstream smoke of non-filter cigarettes*

Cigarette	Ref. no.	Tobacco-specific N-nitrosamines (ng/cig.)		
		NNN	NNK	NAT/NAB
US blend	21	120-950	80-770	140-990
Oriental tobacco	22	3- 19	ND- 4	6- 20
Bright tobacco	22	16- 32	36- 91	40- 90
Turkish tobacco	22	77	59	102
Burley tobacco	22	85-255	70-156	80-225
Black tobacco	22-24	512-625	108-432	200-353

ND, not detected

decompose to reactive diazohydroxides (Fig. 4) which react with cellular components, including nucleophilic centres of DNA. The  $\alpha$ -hydroxylation of NNK at the methylene group leads to methyl-diazohydroxide, as has been shown *in vitro* and also *in vivo* with mice and rats where 7-methylguanine (7-mGua), *O*<sup>6</sup>-methylguanine (*O*<sup>6</sup>-mGua), and *O*<sup>4</sup>-methylthymine appeared in the DNA of those organs that are targets for carcinogenicity of NNK (9); *O*<sup>6</sup>-mGua is known to cause miscoding of DNA (29), leading to oncogene activation (30). In mice, NNK induces lung tumours which contain an activated *K-ras* oncogene (31). *In-vitro* assays with explants of human buccal mucosa, oesophagi, bronchi and peripheral lung have revealed that these tissues have the capability to metabolize NNK and NNN to alkyl-diazohydroxides (Fig. 4), which can react with DNA (9). Figure 5 presents the scheme outlining the link between the tobacco alkaloid, nicotine, and the formation of the DNA adducts that lead to mutation and oncogene activation (30,31).

The second pathway of NNK and NNN metabolism proceeds *via*  $\alpha$ -hydroxylation at



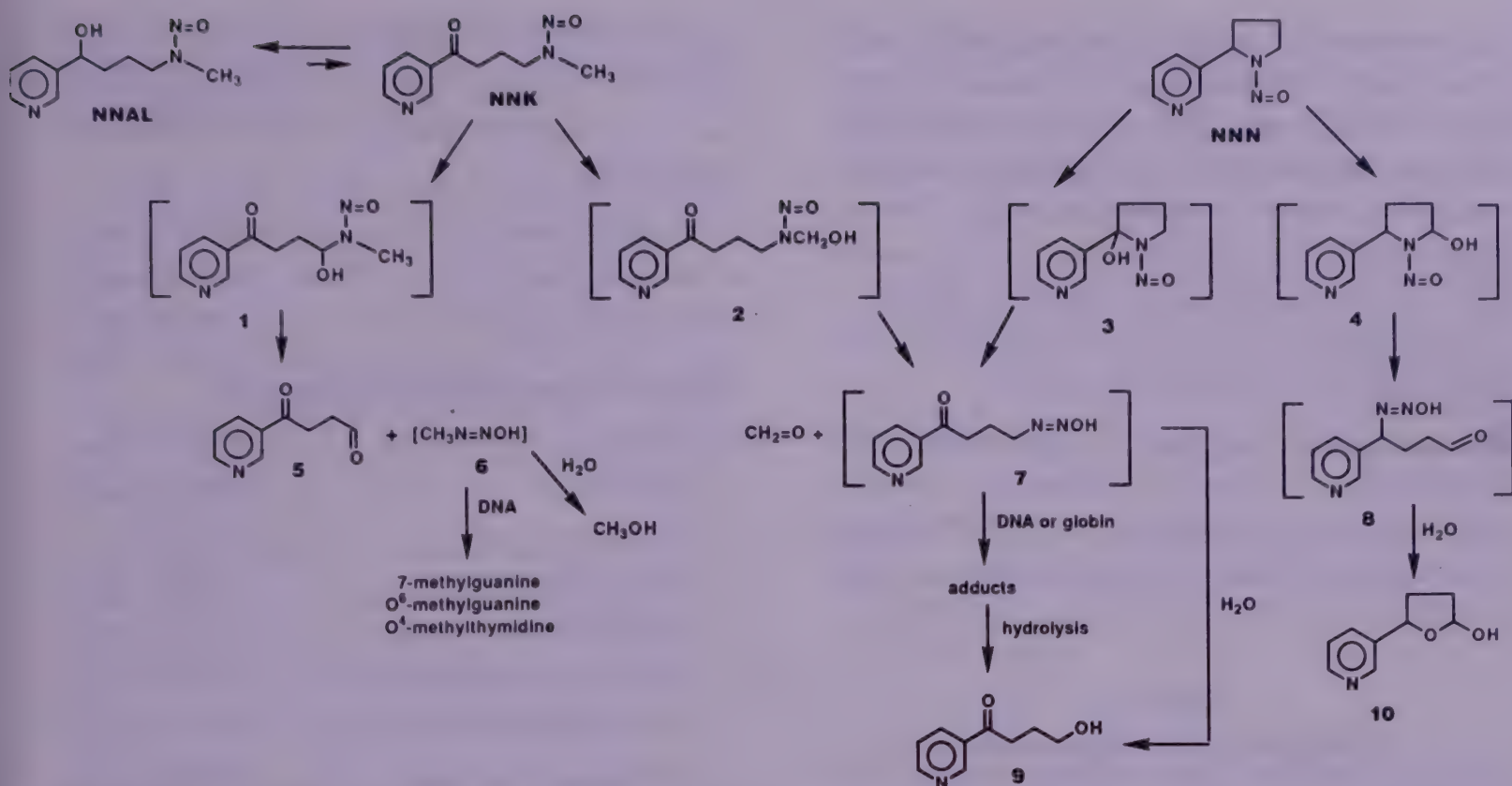


Fig. 4. Metabolic activation of NNK and NNN and presumed intermediates which bind to DNA and protein

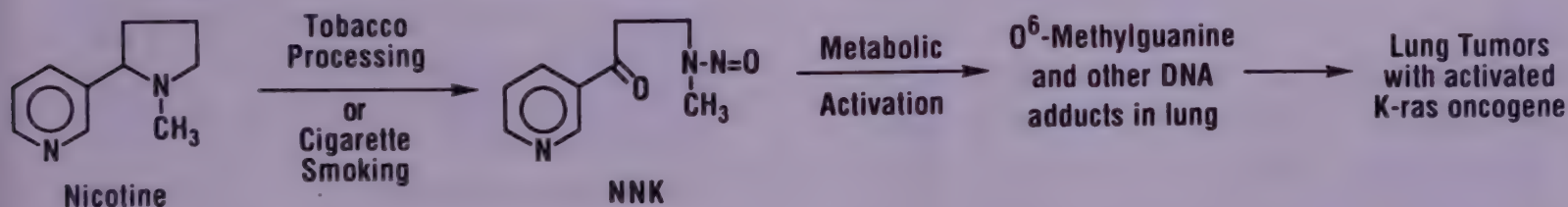


Fig. 5. Scheme linking nicotine *via* NNK to formation of DNA adducts, activation of the *K-ras* oncogene, lung tumours

the methyl group of NNK or 2'-position of NNN, which leads to the intermediate 4-(3-pyridyl)-4-oxobutylhydrazine (compound 7) (Fig. 4), which reacts with DNA as well as with proteins (9). Its reaction with haemoglobin has become the basis of a highly sensitive method developed in our laboratories for human dosimetry of TSNA (32).

The cumulative exposure to the lung carcinogen NNK, inhaled by a smoker of 40 non-filter cigarettes per day over 40 years, amounts to about 1-2 mg/kg (Table 1). In rats, a dose of 30 mg NNK per kg body weight induces malignant tumours (27); 5 mg/kg given to Syrian golden hamsters elicits tumorigenic responses in the respiratory tract (33). These observations have led to the conclusion that TSNA

do make a significant contribution to the increased lung cancer risk of cigarette smokers.

**Aromatic amines:** Cigarette smoke contains traces of at least 16 aromatic amines. Their relative concentrations in the smoke parallel the nitrate content of the tobacco; thus, cigarettes made entirely of black or burley tobacco have higher smoke yields of aromatic amines than do bright tobacco cigarettes (34,35). 2-Toluidine (23-210 ng/cigarette), 2-naphthylamine (0.4-22 ng/cig.) and 4-aminobiphenyl (1.3-5.0 ng/cig.) are the major carcinogenic aromatic amines found in cigarette smoke. The latter two are established human bladder carcinogens (36). Upon metabolic activation, these carcinogenic aromatic amines react with DNA and protein (36,37). It is noteworthy

that smokers of black cigarettes, who inhale smoke with relatively high levels of amines, have a significantly higher risk for bladder cancer than smokers of bright cigarettes, who are exposed to smoke with relatively low levels of amines (38). Nevertheless, the low concentrations of the carcinogenic aromatic amines in cigarette smoke make their role in bladder cancer of cigarette smokers uncertain.

**Miscellaneous organic compounds:** The mainstream smoke of cigarettes contains 20-105 µg of formaldehyde and 10-1400 µg of acetaldehyde (Table 2) (8). Chronic inhalation

**Table 2***Tumorigenic agents in cigarette smoke*

Compounds	Mainstream smoke (per cigarette)
<b>PAH</b>	
Benz[ <i>a</i> ]anthracene	20-70 ng
Benzo[ <i>b</i> ]fluoranthene	4-22 ng
Benzo[ <i>j</i> ]fluoranthene	6-21 ng
Benzo[ <i>k</i> ]fluoranthene	6-12 ng
Benzo[ <i>a</i> ]pyrene	20-40 ng
Chrysene	40-60 ng
Dibenz[ <i>a,h</i> ]anthracene	4 ng
Dibenzo[ <i>a,c</i> ]pyrene	1.7-3.2 ng
Dibenzo[ <i>a,l</i> ]pyrene	present
Indeno[1,2,3- <i>cd</i> ]pyrene	4-20 ng
5-Methylchrysene	0.6 ng
<b>TSNA</b>	
<i>N</i> '-Nitrosonornicotine	3-3700 ng
4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone	ND-770 ng
4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanol	present
<i>N</i> '-Nitrosoanabasine	14-46 ng
<b>Aromatic amines</b>	
2-Toluidine	30-200 µg
2-Naphthylamine	1-22 µg
4-Aminobiphenyl	2-5 µg

Compounds	Mainstream smoke (per cigarette)
<b>Aldehydes</b>	
Formaldehyde	20-105 µg
Acetaldehyde	18-1400 µg
Crotonaldehyde	10-20 µg
<b>Miscellaneous organic compounds</b>	
Benzene	12-73 µg
Acrylonitrile	3.2-15 µg
2-Nitropropane	0.73-1.21 µg
Ethylcarbamate	20-30 ng
Vinyl chloride	1-16 ng
<i>N</i> -Nitrosodimethylamine	0.1-180 µg
<i>N</i> -Nitrosoethylmethylamine	3-13 ng
<i>N</i> -Nitrosodiethylamine	ND-25 ng
<i>N</i> -Nitrosopyrrolidine	1.5-110 ng
<i>N</i> -Nitrosodiethanolamine	ND-36 ng
Quinoline	1-2 µg
Dibenz[ <i>a,h</i> ]acridine	0.1 µg
Dibenz[ <i>a,j</i> ]acridine	3-10 ng
7H-Dibenzo[ <i>c,d</i> ]carbazol	0.7 µg
<b>Radioactive agents</b>	
Polonium-210	0.03-1.0 pCi
<b>Inorganic compounds</b>	
Nickel	0-600 ng
Arsenic	40-120 ng
Chromium	4-70 ng
Cadmium	41-62 ng
Lead	35-85 ng
Hydrazine	24-43 ng

of formaldehyde (14 ppm) and of acetaldehyde (1000-3000 ppm) caused nasal cavity tumours in rats (39). Since rats are obliged to breathe through the nose, these results indicate that the aldehydes are active at the site of application. In smokers who inhale mainstream smoke deeply, therefore carcinogenic effects might be expected in the lungs. Over a period of 40 years, a heavy cigarette smoker (40



cigarettes/day) is exposed to about 58 g of formaldehyde (100 µg/cigarette) and 580 g of acetaldehyde (1000 µg/cigarette).

Cigarette smoke also contains 12-73 µg/cig. of leukaemogenic benzene (40). This finding strengthens epidemiological observations of an elevated risk for leukaemia among long-term cigarette smokers (50-120% above that of nonsmokers), even though it does not prove that benzene contributes to the leukaemia risk of smokers (41).

Table 2 lists a number of other carcinogenic organic constituents of cigarette smoke. The extent to which these agents contribute to the overall increased cancer risk of cigarette smokers has not yet been evaluated.

**Inorganic carcinogens:** Polonium-210 occurs in the smoke at up to 1.0 pCi/cigarette (1). This  $\alpha$ -particle-emitting element is strongly carcinogenic, as evidenced by the induction of tumours of the lung upon its intratracheal instillation in Syrian golden hamsters (42).

**Table 3**

*Probable causative agents for cigarette smoke-related cancers*

Organ(s)	Initiator or carcinogen	Enhancing agents
Lung, larynx	PAH	Catechols (co-carcinogens)
	NNK	
	Polonium-210 (minor factor)	Acrolein, crotonaldehyde (?)
	Acetaldehyde Formaldehyde	
Oral cavity	PAH NNN, NNK	Ethanol
Oesophagus	NNN	
Pancreas	NNK NNAL	
Bladder	2-Naphthylamine 4-Aminobiphenyl	

Polonium-210 concentrations in the lungs of smokers were generally three times higher

than those in the lungs of nonsmokers. The US National Council on Radiation Protection Measurement ascribed about 1% of the risk for lung cancer after 50 years of cigarette smoking to Polonium-210 inhaled with the smoke (43).

Table 2 also lists the levels of inorganic carcinogens that have been discussed as possible contributors to tobacco carcinogenesis (8). Except for nickel (1,44), it is rather unlikely that these inorganic components have a significant role in the etiology of tobacco-related cancer. Table 3 summarizes our present knowledge with regard to those agents that are regarded as established pathogens in smoking-related cancers.

## THE CHANGING CIGARETTE

Two decades of extensive anti-smoking publicity, major efforts in health education and increasing availability of smoke withdrawal clinics have not prevented an increase in cigarette smoking in many parts of the world, and they have lowered cigarette consumption in only some of the developed countries (4). In view of these difficulties, alternative modes of cancer prevention or reduction must be pursued. Effective modification of tobacco products is one approach towards this goal.

By comparison to smokers of plain cigarettes, the long-term smoker of filter cigarettes has a 20-50% reduction in risk for cancer of the lung and for cancer of the upper aerodigestive tract (45). Since an observation period of at least 10 years is required before a valid comparison of cancer risk between smokers of filter cigarettes *vs* plain cigarettes can be made, the presently available epidemiological data do not reflect effects of the more recent changes in the make-up of cigarettes (46). Such changes include perforated filter tips, highly porous cigarette paper, cigarettes containing expanded tobacco with higher filling power and cigarettes of small diameters (45).

Both the toxicity and carcinogenic potency of the smoke are strongly affected by



the types and varieties of tobacco used for cigarettes. For this reason, even plain cigarettes have, over the past three decades, delivered lower smoke yields of tar and nicotine. For example, in 1960, the leading US non-filter cigarette gave smoke yields of 35.1 mg tar and 2.4 mg nicotine (47); in December 1988, the US Federal Trade Commission listed 24.0 mg tar and 1.5 mg nicotine for the same brand; thus, reductions of 30% and 37%, respectively, had been achieved (48).

The only way to experimentally evaluate how recent modifications in cigarette manufacture affect smoke toxicity and/or carcinogenicity is by systematic laboratory tests. Such screening assays must include chemical analyses of cigarette tobacco and its smoke, *in-vitro* bioassays for cilia toxicity and genotoxicity, and longterm assays for tumorigenicity of tars. If indicated, such tests must be followed by long-term inhalation studies.

It has been shown that utilization of the ribs of burley tobacco in blends for cigarettes significantly increases nitrosamine levels because the ribs contain more nitrate than any other portion of the leaf. The higher nitrate levels provide greater nitrosation potential, thus leading to increased smoke yields of volatile and tobacco-specific *N*-nitrosamines (22,25). Another concern is that the addition of certain flavouring agents to the tobacco of low-yield cigarettes may potentiate the toxicity of the smoke.

These examples underscore the importance of non-industrial scientists monitoring changes in the make-up of cigarettes. Between 1987 and 1989, we witnessed the marketing of two new types of cigarettes. One novel development involved a cigarette that 'heats rather than burns tobacco' (49). Although it was conceptually intriguing and technologically exciting, the product failed to gain consumer acceptance. The newest modified cigarette on the market is one that contains tobacco from which more than 90% of the nicotine has been

removed by supercritical extraction with carbon dioxide (50). This development appears to offer potential benefits in that it would reduce the levels of habituating nicotine and the alkaloid-derived, highly carcinogenic *N*-nitrosamines in the smoke. Results of chemical analyses and of bioassays of the smoke of these cigarettes are not yet available.

### FACTORS THAT MODIFY THE CARCINOGENICITY OF CIGARETTE SMOKE

The intake of certain dietary components can potentially modify or counteract the carcinogenic effect of cigarette smoke. Macronutrients, such as fat, have been considered as modifiers of lung cancer risk of cigarette smokers (51,52). More importantly, epidemiological studies have indicated that certain micronutrients, such as carotenes, affect lung cancer incidence rates (52,53). On the basis of these observations, Wattenberg and others have studied the tumour-inhibiting activities of various compounds in laboratory animals (54-56).

Such laboratory studies confirm that the metabolic activation of tobacco smoke carcinogens, such as PAH and TSNA, can be influenced by micronutrients. Specifically, it has been reported that D-limonene and other monoterpenes inhibit the lung tumorigenicity in mice of *N*-nitrosodiethylamine and NNK (55,56). This finding has important implications for tobacco carcinogenesis, since limonene is also a constituent of tobacco and of its mainstream smoke (1-56 µg/cig.) and sidestream smoke (39-467 µg/cig.) (57).

The metabolic activation of NNN and NNK in rats, as well as the methylation of liver DNA by NNK, is inhibited by certain isothiocyanates (58,59). In mice and rats, the metabolic activation of NNK, its methylation of lung DNA, and its lung tumorigenicity are significantly inhibited by feeding of arylalkyl isothiocyanates. The length of the alkyl chain



is of importance in this regard (60-62). These chemopreventive studies in tobacco carcinogenesis are not only of academic interest but may lead to practical measures for the reduction of lung cancer.

## BIOMARKERS IN TOBACCO CARCINOGENESIS

A better understanding of chemical carcinogenesis and the need for risk assessment have stimulated the development of biomarkers as indicators of exposure to environmental carcinogens. For many years, nicotine and cotinine in saliva, blood and/or urine have been utilized as markers of exposure to tobacco products in active and passive smokers. Since 1985, specific tobacco carcinogens, have also been used for dosimetry of their uptake from tobacco smoke.

Metabolic activation of the carcinogenic aromatic amines by *N*-hydroxylation yields hydroxylamines. These species are transported from the liver to the bladder, where they can react with DNA and thus initiate tumorigenesis (63). It has been found that the aromatic hydroxylamines can also form adducts of a cysteine moiety in the  $\beta$ -chain haemoglobin (64). Upon hydrolysis, these adducts revert to the original aromatic amines, which are derivatized, separated by gas chromatography and measured by mass spectrometry. Time-weighted averages then reflect the actual exposure to carcinogenic aromatic amines (62). Such studies have shown that levels of the haemoglobin adduct with the human bladder carcinogen, 4-aminobiphenyl, are significantly higher in cigarette smokers than in non-smokers. Inhalation of smoke from black cigarettes also led to higher levels of 4-aminobiphenyl-haemoglobin adducts than did inhalation of smoke from bright cigarettes (37).

A second method for dosimetry of exposure to smoke carcinogens is determination

of haemoglobin adducts formed with NNN and NNK in cigarette smokers and tobacco chewers. The basic hydrolysis of these adducts leads to the release of 4-hydroxy-1-(3-pyridyl)-1-butanone (compound 9) (Fig. 4). This keto alcohol is derivatized, separated by gas chromatography and analysed by mass spectrometry (32,65).

These biomarker methods are now being utilized in epidemiological studies and are expected to lead to objective data on exposure to cigarette smoke for smokers and perhaps even for involuntary smokers.

## OUTLOOK

As long as society condones cigarette smoking, laboratory studies are needed to provide a more complete understanding of the factors involved in tobacco carcinogenesis. Moreover, studies on the effects of nutrition and of other environmental agents, as well as the need for monitoring the toxicity and tumorigenicity of newly emerging types of cigarettes, require continuing laboratory investigations. Equally important is the development of chemopreventive approaches that will block or suppress the tumorigenic effects of cigarette smoke. Lastly, biomarker methods for objective evaluation of exposure to tobacco carcinogens should be refined. The latter will provide better risk assessment for individuals and for cohorts.

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# Carcinogenic potential of some Indian tobacco products

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Although there is epidemiological evidence to link tobacco use with oral cancer in India, the carcinogenic potential of tobacco products has not yet been established in long-term bioassays. In a study conducted in animal systems with tobacco products commonly used in India, we conclude that (i) certain tobacco products used in India are carcinogenic to animal systems; (ii) the carcinogenicity is enhanced by a commonly used herbicide and by chillie extract; (iii) betel quid containing tobacco extract is less harmful than an extract of tobacco alone; and (iv) *bidi* smoke condensate is also carcinogenic. It is suggested that various modulatory factors may be involved in oral carcinogenesis, and the identification of such factors constitutes an important means of reducing the risk from tobacco.

## INTRODUCTION

Tobacco habits are prevalent in all sections of Indian society, and most consumers begin use at an early age and continue for several decades. The dynamics of tobacco use in the population is described in an earlier paper (see Bhonsle *et al.*, this volume). Tobacco habits in India include smoking of cigarettes, *bidis*, *chuttas*, *chilum* and *hookli*. Tobacco is also chewed, generally with slaked lime or in a betel quid. In rural areas, tobacco is also used as a toothpaste in the form of *gudhaku* and *mishri*. The latter is a pyrolysed product used initially for cleaning teeth but which becomes a habit, especially among women in Maharashtra (1). Several tobacco-containing toothpastes (creamy snuff) have become available commercially and are becoming increasingly popular. Tobacco is also used for inhalation as snuff by a small minority of older people.

A link between tobacco chewing (in betel quid) and oral cancer was suspected as early as 1902 (2), and this was subsequently confirmed (3); however, the carcinogenic potential of

such tobacco products has not yet been established in long-term bioassays. We report here on the carcinogenic potential of some Indian tobacco products in mice, rats and hamsters.

## MATERIAL AND METHODS

**Experimental animals:** Eight-week-old male Swiss mice, 8-week-old male Wistar rats and 8-week-old, male Syrian golden hamsters were treated with various extracts, as described below. Animals were maintained at  $20 \pm 1^\circ\text{C}$  and fed standard laboratory diet (4). They were treated with the preparations described below.

### *Preparation of products and extracts*

**Tobacco extract:** Pandharpuri brand of chewing tobacco (*Nicotiana rustica*) was purchased from a local market and an ethanol extract was prepared by the method of Shah *et al.* (4).

**Betel quid with tobacco:** A water extract of a quid containing two *Piper betle* leaves, 1 g areca nut, a pinch of catechu, slaked lime and 4 g tobacco was prepared by the method of Shirname *et al.* (5).



**Tobacco plus benzene hexachloride:** In order to simulate the human situation, 50 g tobacco were mixed with 100 ml saliva obtained from normal, healthy subjects with no tobacco habit. The mixture was diluted in distilled water and flash-evaporated to obtain a viscous fluid, which was mixed with mouse diet and with 0.625 g benzene hexachloride, a common herbicide, to a final concentration of 125 ppm.

**Chillie extract:** Chillies, (*Capsicum annum* and *C. frutescence*), often used in the Indian diet, were extracted by the method of Nagabhushan and Bhide (6).

**Mishri:** *Mishri* was prepared as described previously (see paper by Bhonsle *et al.*, this volume). An extract was prepared by the method of Kulkarni *et al.* (7) and evaporated to dryness. The residue was dissolved in acetone to give a total of 1 or 2.5 g *mishri* in 20 µl of acetone.

**Bidi smoke condensate:** A solution of *bidi* smoke condensate in dimethyl sulfoxide was prepared as described by Shirname *et al.* (8).

**Snuff:** One popular brand of crude nasal snuff and one of scented nasal snuff were suspended in liquid paraffin for topical application.

**Treatments:** Eight independent experiments were carried out using the products described above.

(i) In the first experiment, 20 male Swiss mice were fed extracts of tobacco or betel quid with tobacco by gavage, five days per week for 16 months. At the end of this period, animals received only a normal diet and were observed until death. Controls received distilled water by gavage and a normal diet. (ii) In the second experiment, 20 Swiss mice received a diet containing 50 g tobacco per kg diet until they were 20 months old. Both the diet and drinking-water were given *ad libitum*. At the end of treatment, they were returned to a normal diet and observed until death. Controls received a

normal diet only. (iii) A further group of 40 Swiss mice received the diet containing tobacco/saliva extract and benzene hexachloride *ad libitum* to the age of 18 months. At the end of treatment, they were returned to a normal diet and observed for life. Groups of 40 mice receiving only 125 ppm benzene hexachloride or only the tobacco/saliva extract or normal diet were used as controls. (iv) A group of 25 BALB/c mice received tobacco extract in the diet and chillie extract in drinking-water (1 mg capsaicin/ml) *ad libitum* until the age of 18 months, after which time they were observed until death. Control groups of 25 mice received only tobacco extract or only chillie extract. (v) Groups of Swiss mice, Wistar rats and Syrian hamsters consisting of 30 animals in each group were fed diets containing 10% *mishri* for 20 months, after which time they were returned to a normal diet and observed until death. (vi) Groups of 30 Swiss mice and Swiss nude mice, a mutant strain that is highly sensitive to skin carcinogenesis (9), were painted on the back skin with 2.5 mg *mishri* extract once a day for five days per week until they were 20 months old and were observed until death. Mice receiving acetone or no treatment served as controls. (vii) 20 Swiss mice were given 1 mg *bidi* smoke condensate by gavage once a day on five days per week for 35 weeks, then observed until death. Controls received either 0.1 ml dimethyl sulfoxide or no treatment. (viii) Groups of 20 hamsters were treated topically on the cheek pouch epithelium with 20 mg crude or scented snuff on five days per week for a period of 21 weeks, at which time they were sacrificed. A positive control group of 20 hamsters received 7,12-dimethylbenz[*a*]anthracene (DMBA), a standard carcinogen, and a further control group received no treatment.

**Histological methods:** All the control and treated animals from different groups were killed by cervical dislocation and dissected carefully. Lung, liver, kidney and other grossly abnormal tissues were fixed in 10% formalin,



processed by routine histological techniques and embedded in paraffin. Paraffin sections, 6  $\mu$ m thick, were cut and stained with haematoxylin and eosin for microscopic examination.

## RESULTS

Tobacco extract administered to Swiss mice by gavage or in the diet induced lung and liver

carcinomas in 10/20 and 8/18 treated animals, respectively (Table 1). Only one mouse in the control group developed a lung tumour. The extract of betel quid with tobacco was less tumorigenic; however, simultaneous treatment with benzene hexachloride or with chillie enhanced the tumorigenic effect of tobacco. In animals treated with tobacco extract + BHC,

**Table 1**

*Tumour incidence in Swiss and BALB/c male mice treated with betel quid and tobacco (BQT), tobacco (T) alone or in combination with benzyl hexachloride (BHC) or with chillie*

Group	Effective no. of mice <sup>a</sup>	Route	Tumour incidence (months)			Total tumour incidence
			9-14	15-20	21-25	
<b>Swiss</b>						
Untreated	20			0/6	1/14	1/20 (5%)
BQT	18	Gavage		1/10	3/8	4/18 (22%)
T	20	Gavage		8/15	2/5	10/20 (50%)
T	18	Diet			8/18	8/18 (44%)
T+BHC	40	Diet	14/20	20/20	—	34/40 (85%)
BHC	35	Diet	0/10	7/9	14/16	21/35 (60%)
<b>BALB/c</b>						
T	15	Diet	0/6	2/9	—	2/15 (13%)
T+chillie	15	Diet	0/3	4/12	—	4/15 (27%)
		Drinking- water				
Untreated	20	—	0/6	1/10	—	1/20 (5%)
Chillie	23	Drinking- water	2/14	0/9	—	2/23 (9%)

<sup>a</sup>Number of mice that survived beyond eight months

**Table 2**

*Lung and stomach papilloma incidences in mice, rats and hamsters kept on 10% mishri diet*

Species	Treatment	Age group (months)		Total tumour incidence
		12-18	19-25	
Mice	Untreated		1 lung	3/27 (11%)
			2 stomach	
	Mishri		2 lung	14/26 (54%)
			12 stomach	
Rats	Untreated	0/6	0/19	0/25
	Mishri	2/6	8/21 stomach	10/27 (37%)
Hamsters	Untreated	0/6	2/20 stomach	2/23 (9%)
	Mishri	3/10	9/18 stomach	12/28 (43%)

**Table 3***Skin lesions induced by daily painting of mishri extract on the back skin of Swiss and Swiss nude mice*

Strain	Treatment	Incidence of lesions			Total tumour incidence
		Hyperplasia	Papilloma	Carcinoma	
Swiss	Acetone (20 $\mu$ l)	8/30 (27%)	0	0	0
	Mishri (2.5 mg/day)	14/30 (47%)	0	0	0
Swiss nude	Acetone (20 $\mu$ l)	19/23 (83%)	0	0	0
	Mishri (1 mg/day)	13/21 (61%)	6	1	7/21 (33%)
	Mishri (2.5 mg/day)	9/17 (53%)	6	0	6/17 (35%)

**Table 4***Tumour incidence in Syrian golden hamsters treated with snuff inhalation*

Group of animals	No.	Papilloma		Papillomas per hamster			
		Cheek pouch	Stomach	0.5-1.0 mm	1-1.5 mm	2-4 mm	Total
Untreated	15	—	—	—	—	—	—
DMBA	20	10/15 (66%)	15/15 (100%)	9.9	6.8	—	16.7
Crude snuff	20	0/20	17/20 (85%)	12.7	1.0	—	13.7
Scented snuff	20	0/20	15/20 (75%)	6.7	1.5	1.0	9.2

hepatocarcinomas were observed, and the increase in tumour incidence was significant ( $p < 0.05$ ). In the tobacco + chillie group, an increased incidence of lung adenocarcinomas was observed ( $p < 0.1$ ).

Feeding of 10% *mishri* in the diet to mice, rats and hamsters increased the incidence of papillomas in the lung and stomach in all the three species over those in controls (Table 2). *Mishri* extract induced skin papillomas in Swiss nude mice but not in Swiss mice, although hyperplasia was seen in 14/30 animals (Table 3).

Neither type of snuff induced cheek-pouch papillomas in treated hamsters, but forestomach papillomas were observed in 17/20 and 15/20 animals (Table 4).

Among BALB/c mice treated with *bidi* smoke condensate, 7/15 developed tumours, two of which were carcinomas (one of the

stomach and one of the oesophagus). The other tumours were four liver haemangiomas and a papilloma of the stomach. No tumour was seen in controls.

## DISCUSSION

We have demonstrated the carcinogenicity to experimental animals of an extract of the tobacco commonly used for chewing in India, and have shown that the carcinogenicity is enhanced by a commonly used herbicide (benzene hexachloride) and by chillie (a common component of the Indian diet). The finding that the extract of betel quid containing tobacco was less carcinogenic to mice after gavage than tobacco extract may be attributed to a chemopreventive effect of betel leaf and *catechu*, two important constituents of betel quid, which are proven antimutagens (10,11). Betel leaf has been shown to be anticar-



cinogenic as well (12). *Mishri* appears to be a weak carcinogen, since it induced only benign tumours in the skin of mice and in the forestomach of mice, rats and hamsters. We further found hamster cheek-pouch mucosa to be more resistant than forestomach mucosa. *Bidi* smoke condensate induced two carcinomas, one of which was in the oesophagus. These data indicate the carcinogenicity of many of the tobacco products used by the Indian people.

The carcinogenicity of cigarette smoke, which contains two major classes of carcinogens, namely polycyclic aromatic hydrocarbons and tobacco-specific *N*-nitrosamines (TSNA), has been adequately proven (13-15); we report here on the carcinogenicity of *bidi* smoke condensate. *Bidi* smoke is reported to contain both polycyclic aromatic compounds as well as TSNA (16,17). The carcinogenicity in experimental animals of smokeless tobacco products used in the USA and Europe has also been reported in recent years (13,18), and we reported earlier on the carcinogenicity of chewing tobacco in mice (4) and the presence of polycyclic aromatic hydrocarbons and TSNA in snuff, which are initiator and pro-

moter types of compounds, respectively (16,17). Tobacco used for chewing, in the crude or in processed form, contains considerable quantities of TSNA (19,20), two of which, *N*-nitrosonornicotine and 4-(methyl-nitrosamino)-1-(3-pyridyl)-1-butanone (NNK), are potent carcinogens in mice, rats and hamsters (18,21). These two compounds induce tumours in lung, liver and stomach; however, relatively few tumours are observed in the oral mucosa. Recently, we succeeded in inducing cheek-pouch tumours in hamsters by adding hydrogen peroxide simultaneously with NNK; *in vitro*, peroxide radicals appear to be formed transiently in the oral cavity during the chewing of tobacco (22).

Although the oral mucosa of tobacco chewers is bathed in saliva containing TSNA (74-440  $\mu\text{g/day}$ ), other modulatory factors, such as spices, nutritional status and concurrent exposure to other carcinogens (through air, water and occupation) may influence transformation of the normal oral mucosa to malignant tissue. The identification of such modulators is an important aspect of reducing the cancer risk of tobacco users.

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# Toxic effects of exposure to tobacco among *bidi* rollers

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Workers employed in *bidi* rolling receive prolonged exposure to unburnt tobacco. Since smokeless tobacco use is known to be associated with a high incidence of oropharyngeal cancers, *bidi* rollers were monitored for the biological effects of occupational exposure to tobacco. Specific exposure was determined by estimating cotinine levels, while nonspecific exposure to electrophilic agents was assessed by estimating urinary thioethers. Urinary mutagenicity was determined using the Ames assay, and micronucleus frequency in exfoliated buccal epithelial cells was recorded as a genotoxic endpoint. Unexposed subjects with similar socioeconomic status were used as controls. *Bidi* rollers exhibited significantly higher urinary thioether levels and micronucleated cell frequency. An increased number of urine samples contained mutagenic nitrosatable species and promutagenic compounds, with a resultant increase in the mean number of revertants as compared to controls. These results indicate that *bidi* rollers are at a high risk for genotoxic hazards due to occupational exposure to unburnt tobacco.

## INTRODUCTION

Smokeless tobacco use is causally associated with oral and oropharyngeal cancers (1,2). It is estimated that in India, one-third of new cancer cases are related to tobacco habits (3), the most common habit being *bidi* smoking. *Bidi* is made (see paper by Bhonsle *et al.*, this volume) by hand-rolling 250-500 mg, sun-dried tobacco flakes in a dried *temburni* leaf (*Diospyros melanoxylon*). Blends of *Nicotiana tabacum* cultivated in India are used as filler.

In Bombay, over 40 000 women are engaged in *bidi* rolling and thus receive chronic exposure to large amounts of unburnt tobacco. However, no information is available about their occupational health hazards, since this is a home-based, unorganized industry. In the present study, female *bidi* rollers were monitored for possible ill-effects of their occupation. Salivary and urinary cotinine levels were determined for tobacco-specific exposure, and, since exposure to electrophilic moieties

increases the excretion of thioethers in urine (4), urinary thioether levels were estimated as an index of total electrophilic burden. Urinary mutagenicity was determined by the Ames assay (5), and the frequency of micronucleated buccal epithelial cells (6) was assessed as a further genotoxic endpoint.

## MATERIAL AND METHODS

**Subjects:** Thirty-two female *bidi* rollers who were nonusers of tobacco were selected for this investigation (Fig. 1). Nonusers were chosen in order to clearly delineate the effects of occupational exposure. Information regarding their age, diet, number of *bidis* rolled per day, years of exposure and medical history was recorded. Twenty-six age-matched women who were not *bidi* rollers and had no tobacco habit served as controls.

**Sampling:** Two to eight ml saliva samples were collected after thorough rinsing of the mouth





Fig. 1. Female *bidi* rollers at work

and were centrifuged at 2000 rpm for 10 min to remove cellular debris. Eight-hour urine samples (~500 ml) starting with early-morning voided sample were collected. Saliva and urine samples were stored without preservative at  $-20^{\circ}\text{C}$  until assayed. Buccal smears were taken by gently rubbing a moistened wooden tongue depressor over the inner aspect of each cheek. Scrapings were spread on labelled glass slides; the slides were air-dried, fixed in methanol for 5 min and stored at  $4^{\circ}\text{C}$  until further study.

**Estimation of cotinine:** Cotinine levels were estimated using the method described by Peach *et al.* (7). One ml of saliva or urine sample was added to a tube containing 4M acetate buffer at pH 4.7 and reacted by the sequential addition at 15-sec intervals of freshly prepared 10% aqueous potassium cyanide, 10% aqueous chloramine T and 1% diethyl thiobarbituric acid in acetone:water (1:1 v/v). A positive result was indicated by the appearance of a pink colour within 20 min, after which the reaction product was extracted into 2 ml ethyl acetate. The optical density was measured at 532 nm using a Uvicon double-beam spectrophotometer, and the concentration of nicotine metabolite was calculated using cotinine as standard. The lower limit of sensitivity of this method was found to be  $0.5\text{ }\mu\text{g/ml}$ . All urine samples that gave a negative result were re-tested after 100-fold concentration.

**Estimation of thioethers:** The method of Savolainen *et al.* (4) was used. Five ml of urine sample were acidified with 4N hydrochloric acid and extracted with 20 ml ethyl acetate. The organic fraction was evaporated to dryness, and the residue was dissolved in 2 ml distilled water. One ml of this extract was hydrolysed in the presence of 4N sodium hydroxide in a boiling water bath for 50 min, and the tubes were cooled immediately in ice. To 2 ml of 0.5M phosphate buffer (pH 7.1), 0.25 ml of hydrolysate and 0.3 ml of 5,5'-dithiobis (2-nitrobenzoic acid) solution were added. Absorbance was read at 412 nm using a Uvicon double-beam spectrophotometer. Correction was done for the colour of urine, and the concentration of thioethers was derived from the standard curve obtained with *N*-acetyl-L-cysteine (4).

**Concentration of urine:** Urine samples were filtered through Whatman No. 1 filter paper and passed through a glass column (1.5 cm x 10 cm) containing 10 g XAD-2 resin. Before being loaded onto the column, the resin was washed sequentially with 100 ml each of acetone, acetone:water (1:1), methanol and water. After the sample had been passed through the column (percolation speed, 3-5 ml/min), the column was washed twice with water before elution with 15 ml acetone followed by 20 ml water (8). The concentrates were lyophilized and solubilized in dimethyl sulfoxide (0.4 ml/100 ml urine).

**Salmonella/microsome mutagenicity assay:** *Salmonella typhimurium* TA98 and TA100 strains were kindly provided by Professor B.N. Ames (Berkeley, USA). The modified preincubation procedure of Malaveille *et al.* (9) was used to test urine concentrates for mutagenicity. Three testing protocols were followed: (i) without treatment, (ii) following treatment with 200 units of  $\beta$ -glucuronidase and (iii) following treatment with 0.2M sodium nitrite at pH 2. The samples were assayed in the presence or absence of rat liver S9.



Each assay sample consisted of 100 µl of two-fold concentrated bacterial culture ( $2-4 \times 10^8$  cells), 100 µl S9 mix and appropriate amounts of urine concentrate (0.3-1.25 ml equivalents). One ml of S9 mix contained 100 µl 80 mM  $\text{MgCl}_2$ , 100 µl 8 mM  $\text{NADP}^+$ , 100 µl 50 mM glucose-6-phosphate, 300 µl 0.25 M Sorensen phosphate buffer (pH 7.4) and 50 µl of S9 (9000 g preparation) from the livers of Aroclor 1254-treated male Sprague-Dawley rats. Incubation was carried out for 90 min at 37°C. In experiments without S9, equivalent amounts of phosphate buffer (pH 7.4) were added. After addition of 2 ml of histidine-poor soft agar, the mixture was plated onto minimal glucose agar, as described by Maron and Ames (5). Each experiment was carried out in duplicate.

**Assessment of micronucleus frequency:** The acridine orange fluorescence method of Hayashi *et al.* (10) was followed. Briefly, fixed slides were stained with 0.1% acridine orange for 3 min in 0.7M Sorensen buffer, rinsed thrice in buffer, air-dried and mounted. Observations were made under a Carl-Zeiss fluorescence microscope with a band-pass filter (450-490 nm excitation; 550-565 nm emission range). Slides were initially scored at 40X, and the presence of micronuclei was confirmed at 100X magnification. A minimum of 1000 buccal epithelial cells was screened for the presence of micronuclei in each slide.

**Creatinine estimation:** Creatinine was determined by the alkaline picrate method (11). Values for urinary cotinine, thioethers and mutagenicity were expressed per mole of creatinine in order to compensate for differences in concentration of the urine.

**Statistical analysis:** Levels of cotinine and thioethers and micronucleus frequency were compared with those in controls using Student's *t* test for comparison of means from two independent samples. When the assumption of equality of the variance of the compared groups did not hold, approximation due to variance of Cochran to Behrens-Fisher solution was used to compare the means. The Mann-Whitney-Wilcoxon test was applied to compare the distribution of the number of revertants induced by urine samples from *bidi* rollers and control subjects.

## RESULTS

The mean ages of the *bidi* rollers and controls were  $25.6 \pm 2.1$  and  $32.2 \pm 2.6$  years, respectively. Workers were engaged in *bidi* rolling for 4-6 h/day, seven days per week. Each worker rolled 500-1000 *bidis* and reportedly handled 225-450 g of tobacco each day.

**Metabolic indicators of exposure:** As shown in Table 1, detectable levels of cotinine were found in the saliva and urine only of *bidi* rollers. The mean urinary thioether levels in *bidi*

Table 1

Levels<sup>a</sup> of cotinine, thioether and micronucleus frequency in *bidi* rollers and controls

Group	Parameter			
	Salivary cotinine (µg/ml)	Urinary cotinine (mmol/mol creatinine)	Urinary thioethers (mmol/mol creatinine)	Micronucleus frequency in buccal epithelial cells (%)
Controls	ND (0/15)	ND (0/26)	$1.83 \pm 0.34$ (26/26)	$0.48 \pm 0.07$ (17/17)
<i>Bidi</i> rollers	$0.84 \pm 0.26$ (6/32)	$0.09 \pm 0.03$ (9/18)	$4.59 \pm 0.52^*$ (18/18)	$0.68 \pm 0.06^{**}$ (29/29)

<sup>a</sup>Mean  $\pm$  SE; figures in parentheses indicate number of positive/total samples; ND, not detectable

\* $p < 0.001$ ; \*\* $p < 0.05$



**Table 2**  
*Urinary mutagenicity<sup>a</sup> in bidi rollers and controls with no tobacco habit*

Group	Metabolic modulator											
	None		S9		$\beta$ -Glucuronidase		$\beta$ -Glucuronidase + S9		Nitrite		Nitrite + S9	
	TA98	TA100	TA98	TA100	TA98	TA100	TA98	TA100	TA98	TA100	TA98	TA100
Controls	0.31	—	0.69	0.88	—	2.89	0.63	1.82	1.26	5.67	0.47	2.33
	0.91	—	—	0.65	0.26	—	—	0.78	3.50	18.61	1.82	8.95
	—	—	0.74	2.42	0.41	1.39	—	1.19	1.02	5.28	0.78	3.11
	—	—	1.66	2.37	—	3.32	—	1.25	2.84	18.01	1.66	8.77
	—	—	—	1.46	—	—	—	—	1.99	18.15	0.77	7.10
	—	—	—	2.40	0.21	—	—	—	1.61	6.21	0.63	2.62
<i>Bidi</i> rollers	—	—	—	—	0.82	—	—	1.95	2.82	1.13	0.77	0.59
	1.54	—	1.67	7.18	—	—	—	16.02	6.28	—	1.92	—
	0.72	—	1.78	0.24	0.48	0.13	—	0.23	1.20	—	2.22	0.58
	1.90	—	—	0.76	1.62	0.52	—	2.85	8.56	10.08	7.23	15.03
	1.53	—	0.38	0.77	—	—	—	1.66	2.93	2.34	2.31	3.61

<sup>a</sup>No. of revertants  $\times 10^{-6}$ /mol creatinine

—, non-mutagenic

rollers were significantly greater than those in controls ( $p < 0.001$ ).

**Mutagenicity studies:** There were marked differences in the type of mutagenicity as well as the number of revertants induced by urine samples from *bidi* rollers and controls (Table 2). Occupational exposure to tobacco resulted in increased mutagenicity in TA98 in the absence of metabolic activation, but no mutagenic activity was detected in TA100. Increased mutagenicity to TA98 was also seen after treatment of the urine samples with sodium nitrite or  $\beta$ -glucuronidase in the absence of S9. In the urine of *bidi* rollers, metabolic activation of  $\beta$ -glucuronidase-treated samples with S9 increased their mutagenicity to TA100. A statistically significant increase ( $p < 0.04$ ; Mann-Whitney-Wilcoxon test) in mutagenicity to TA98 was observed after treatment with nitrite in the presence of S9.

**In-vivo genotoxicity:** A statistically significant increase in percent micronucleated buccal epithelial cell frequency was seen in *bidi*

rollers as compared to controls ( $p < 0.05$ ; Table 1).

## DISCUSSION

Cotinine was detected only in urine and saliva samples from *bidi* rollers. The mean levels were several-fold higher than those reported in unexposed individuals (12) or passive smokers (13), indicating that *bidi* rollers absorb substantial amounts of nicotine. *Bidi* rollers also showed a significant increase in urinary thioether excretion and in the frequency of micronucleated buccal epithelial cells as compared to controls.

Occupational exposure to mutagens was evident from increased mutagenicity of urine samples from *bidi* rollers to TA98 in the absence of S9. The finding that this activity diminished after treatment of samples with  $\beta$ -glucuronidase suggests that glucuronide conjugates contributed to the direct mutagenicity to TA98. The mutagenicity of samples treated with  $\beta$ -glucuronidase and S9 to TA100



shows that the  $\beta$ -glucuronidase conjugates are activated metabolically to base-pair substitution-type mutagens. The significant increase in mutagenicity to TA98 of samples treated with sodium nitrite, with or without metabolic activation implies that *bidi* rollers excrete higher levels of nitrosatable pro-mutagens than controls.

Since tobacco is a complex mixture, it is not possible to specify the chemicals that are responsible for the observed clastogenicity to buccal epithelial cells. However, a relationship appears to exist between increased electrophilic and mutagenic burden and micronucleus frequency. This biological assessment points towards the genotoxic hazards of

occupational exposure to tobacco among *bidi* rollers. So far, no clinical or epidemiological observations on health hazards to *bidi* rollers have been reported. In the light of the present findings, such studies are desirable.

### Acknowledgments

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# Correlation between histopathology and flow cytometry of oral leukoplakia and oral cancer

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Conventional methods of assessing the cancer potential of precancerous lesions have met with limited success. In recent times, the successful application of flow cytometric methods to oesophageal cancers, which detect DNA content and the percentage of cells in G<sub>2</sub> and S phase of cell cycle, suggests that such methods could be utilized to assess the malignant potential of oral precancerous lesions. We studied three oral leukoplakias using histopathology and flow cytometry to find out which dysplastic lesions progress to carcinoma. The preliminary results are encouraging.

## INTRODUCTION

The inability to predict accurately which leukoplakic lesions with dysplastic changes will progress to malignancy has long perplexed pathologists and clinicians alike (1-3). The World Health Organization has struggled with this problem since 1967 when it established the Collaborating Centres for Oral Precancer. This extensive international effort resulted in the publication in 1978 of their classic article: 'Definition of Leukoplakia and Related Lesions: An Aid to Studies on Oral Precancer'(4). This group defined leukoplakia as a white patch or plaque which cannot be characterized clinically or pathologically as any other disease. It was emphasized that the term was unrelated to the presence or absence of epithelial dysplasia. This definition allowed investigators to use the consistent terminology.

Individual cellular changes are referred to as atypia, while a generalized disturbance of the epithelium is called dysplasia (3). In 1969, Smith and Pindborg published an excellent monograph which clearly depicted photographically 12 histopathological changes in epithelial cells which herald the subsequent

development of carcinoma. These changes are: loss of polarity of basal cells, the presence of more than one layer of cells having cells with a basaloid appearance, an increase in the nuclear-cytoplasm ratio, drop-shaped rete pegs, irregular epithelial stratification, an increased number of mitotic figures (a few abnormal mitoses may be present), the presence of mitotic figures in the superficial half of the epithelium, cellular pleomorphism, and keratinization of single cells or cell groups in the prickle cell layer (stratum spinosum) (5).

The indictment of tobacco as a carcinogenic agent initially came into scientific prominence with the first case-control study of lung cancer and cigarette smoking by Wynder and Graham in 1950 (6). Carcinoma *in situ* was produced experimentally in the buccal mucosa of protein-deficient baboons by Hamner and Reed in 1972, using a mixture of fresh betel leaves, areca nuts, slaked lime and tobacco for 42 months (7). Many studies throughout the world have now verified that tobacco is a carcinogenic agent (1,3,8,9). The longest, most thoroughly documented, continuous epidemiological study of oral precancer and cancer is



**Table 1**  
*Malignant transformation of oral lesions in the 10-year follow-up study<sup>a</sup>*

Previous diagnosis	Ernakulam district		Srikakulam district	
	No.	New oral cancers detected	No.	New oral cancers detected
Leukoplakia	410	9	302	1
Homogeneous	352	6	278	1
Nodular	14	3	1	—
Ulcerated	44	—	23	—
Preleukoplakia	389	2	342	—
Submucous fibrosis	44	1	5	—
Lichen planus	332	1	18	—
Leukokeratosis nicotina palati/palatal changes	65	—	3438	10
Normals	6160	—	3037	—

<sup>a</sup>Source: ref. (10)

that conducted by Mehta's group at the Tata Institute of Fundamental Research (1,10).

One of the most significant products of their investigations has been the report of incidence rates of oral cancer and the natural history of oral precancerous lesions in a 10-year follow-up study of Indian villagers, published in 1980 (10). This study of 10 287 villagers from the Ernakulam district of Kerala, 10 071 from the Bhavnagar district of Gujarat and 10 169 from the Srikakulam district of Andhra Pradesh was conducted (covering the years 1969-77) following an initial three-year base-

line study involving detection of oral cancer and oral precancerous conditions in house-to-house surveys. One of the most important objectives of the 10-year follow-up was to determine the malignant potential of oral precancerous lesions by measuring their rate of malignant transformation. Table 1 shows the number of lesions that were followed and the number of new oral cancers detected among the precancerous lesions. Nodular leukoplakia exhibited the highest malignant transformation — 20% (3 out of 15 cases in Ernakulam and Srikakulam districts, Table 1).

**Table 2**  
*Clinical behaviour of 90 dysplastic lesions in the 10-year follow-up study according to habits<sup>a</sup>*

Clinical behaviour	No.	%	No habit	Smoking habit (conventional)	Chewing habit	Mixed habit	Reverse smoking
Progressed to oral cancer	6	7%	—	1	3	2	—
Persistent	45	50%	—	5	6	1	33
Regressed	12	13%	—	4	4	4	—
Change in clinical characteristics	27	30%	1	8	3	1	14
Total	90		1	18	16	8	47

<sup>a</sup>Source: ref. (10)



It is generally assumed that epithelial dysplasia is a precursor of carcinoma (8). Table 2 demonstrates the clinical behaviour of 90 dysplastic lesions in a 10-year follow-up study, according to tobacco habits. Six cases progressed to oral cancer, giving the malignant transformation rate of 7%. Some 50% of the dysplastic lesions remained clinically persistent. Complete regression was observed in 13%, and 30% of the lesions changed their clinical characteristics. Among these latter 27 cases, 16 were palatal lesions for which there was a change in clinical classification. For most of the remaining cases, the change was between homogeneous and ulcerated leukoplakias (10).

Table 3 shows the malignant transformation of the 90 oral dysplastic lesions, according to the clinical diagnosis in the base-line study. Three nodular leukoplakias out of 15 transformed to cancer; among six submucous fibrosis and lichen planus cases, one each exhibited malignant transformation. The rate of malignant transformation was 7% for all 90 lesions (10).

The main conclusions of this study were: (i) oral cancer and oral precancerous lesions occurred solely among those persons who practised tobacco habits in one form or another,

and (ii) oral cancer was always preceded by some kind of precancerous lesion (10).

We are left with a perplexing question — why do some of these chronic tobacco users develop cancer, while others, who use tobacco in the same form over a similar duration of time, do not? We have postulated that a possible answer may lie in the differences in patients' immunological systems, specifically the absence of enough active thymus tissue to produce an effective T-lymphocyte response to overcome the cancer (11).

At the University of Tennessee, Memphis, we studied 30 patients, utilizing medical history and computerized tomography (CT) scans, to develop a base-line of thymic conditions, comparing normal controls with head-and-neck cancer patients. Our preliminary results with five patients with cancer in the tonsil, pharynx, larynx or cribriform sinus showed that these patients exhibited either complete absence or marked reduction of thymic tissue on CT scans. This finding, in early cancer cases who had received no form of therapy at the time of CT scanning, is certainly dramatic. This procedure could serve as a possible screening mechanism to predict which leukoplakias may progress to cancer. However, such a procedure is both expensive and

**Table 3**  
*Clinical diagnosis of 90 oral epithelial dysplastic lesions<sup>a</sup>*

Clinical diagnosis	No. of cases	Malignant transformation	
		No.	%
Leukoplakia, homogeneous	38	1	3
Leukoplakia, nodular	15	3	20
Submucous fibrosis	6	1	17
Lichen planus	6	1	17
Other lesions <sup>b</sup>	25	—	—
Total	90	6	7

<sup>a</sup>Source: ref. (10)

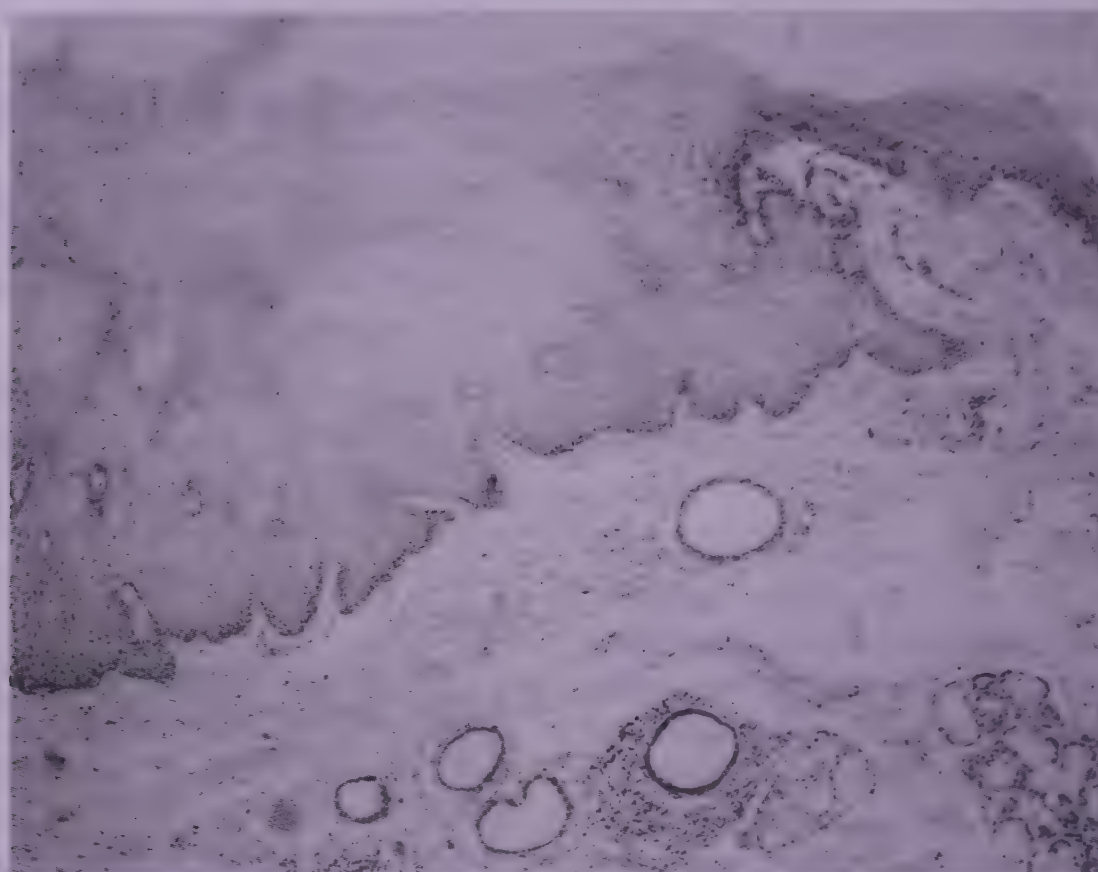
<sup>b</sup>Preleukoplakia, leukoplakia ulcerated, atrophic area, leukokeratosis nicotina palati



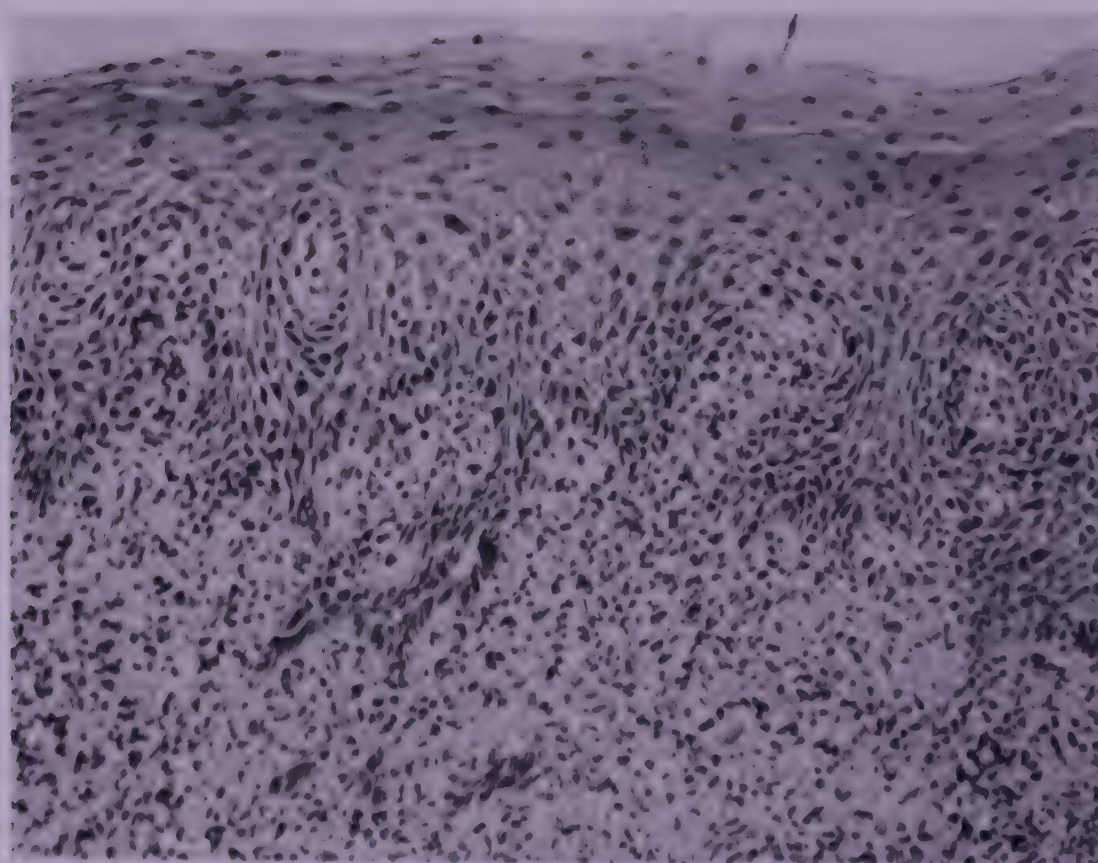
requires the availability of high-grade technology (11).

More often, the pathologist is faced with a leukoplakic lesion that may run the gamut

from epithelial hyperplasia with hyperparakeratosis (Fig. 1) to early dysplastic changes (Fig. 2) or marked dysplasia progressing to carcinoma (Fig. 3). Even with careful



*Fig. 1.* Epithelial hyperplasia with hyperparakeratosis



*Fig. 2.* Early dysplastic changes



clinical differentiation and application of the acknowledged 12 histopathological criteria for

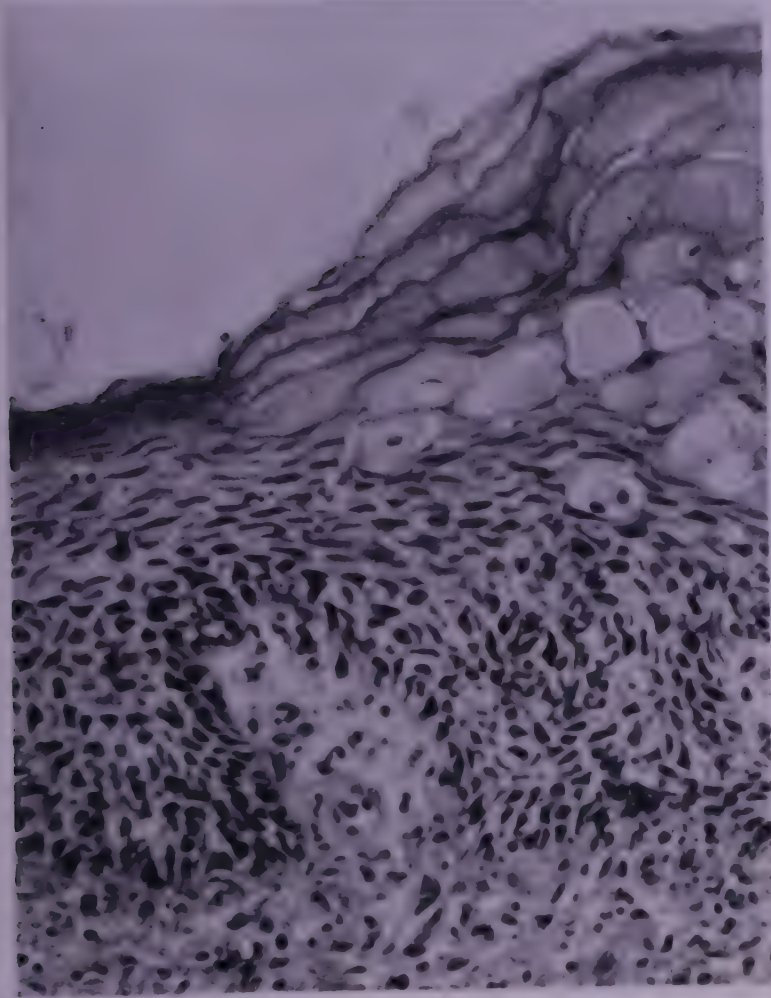


Fig. 3. Marked dysplasia progressing to carcinoma

epithelial dysplasia, the pathologist is often left to rely on 'gut feeling' as to whether a leukoplakic lesion will progress to cancer or not.

A more promising approach has been reported by Reid *et al.* (12) regarding the correlation between flow cytometry and histopathology in detecting patients who are at risk for developing adenocarcinoma of the oesophagus. His group used flow cytometry and histopathology to evaluate 317 biopsy specimens from 64 consecutive patients who were in a cancer surveillance programme for Barrett's oesophagus. Specimens from 10 patients had aneuploid cells, 9 of which demonstrated dysplasia or cancer or both. Twenty patients had G2/tetraploid fractions greater than 6%; all of these 20 specimens were biopsied from patients who had cancer or dysplasia or indefinite dysplasia.

All patients with dysplasia or adenocarcinoma exhibited evidence of genomic instability (aneuploidy) or abnormalities of mucosal proliferation by flow cytometry, even when the dysplasia was focal or difficult to recognize histopathologically. The authors concluded that flow cytometry is capable of detecting alterations in DNA content or proliferation, or both, which are present at high frequency in Barrett's dysplasia and carcinoma of the oesophagus (12).

## MATERIAL AND METHODS

We have commenced a study to determine if flow cytometry and histopathological correlation can be utilized to predict which oral leukoplakias will progress to carcinoma.

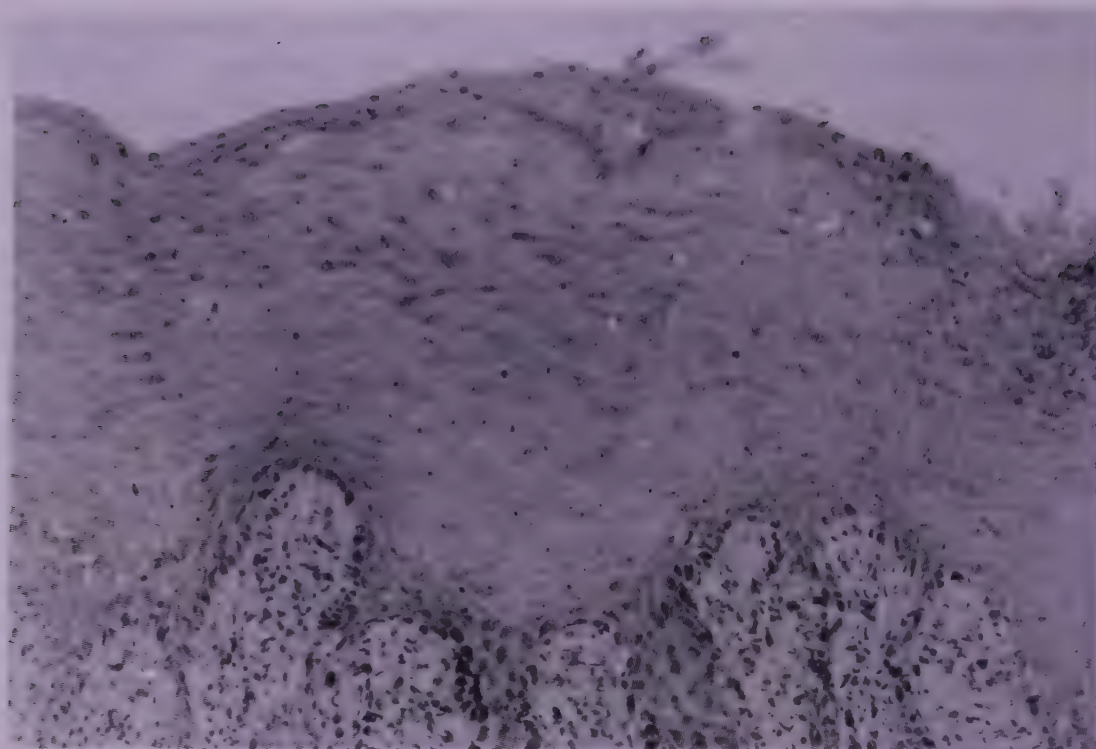
Biopsy tissue specimens from three leukoplakic lesions in three patients were fixed in 10% buffered formalin, dehydrated in ascending ethanol concentrations, embedded in paraffin blocks, sectioned at 6  $\mu$ m, and stained with haematoxylin and eosin. These tissues were removed from the paraffin blocks, minced in Hank's salt solution with gentamicin, passed three times through a #40 wire-mesh sieve, and stained with propidium iodide (which has an affinity for DNA), prior to flow cytometry. Flow cytometry was performed on a Coulter Profile. Data were collected and analysed on an IBM computer with cytologic software (13).

## RESULTS

**Case #1:** This patient was a 31-year old white male with a past history of heavy smoking. He had a 4 x 4 mm painless, white lesion around the attached gingiva of the palate. Microscopically, the lesion demonstrated hyperparakeratosis and mild epithelial dysplasia in the form of hyperchromatic nuclei, variation in the nuclear-cytoplasmic ratio, spindle shaped nuclei in the basal-cell layer and irregular rete peg formation (Fig. 4).

The flow cytometry analysis is illustrated in Figure 5: GO:G1 was 58.6%, G<sub>2</sub>:M was





*Fig. 4.* Hyperparakeratosis and mild epithelial dysplasia in case 1

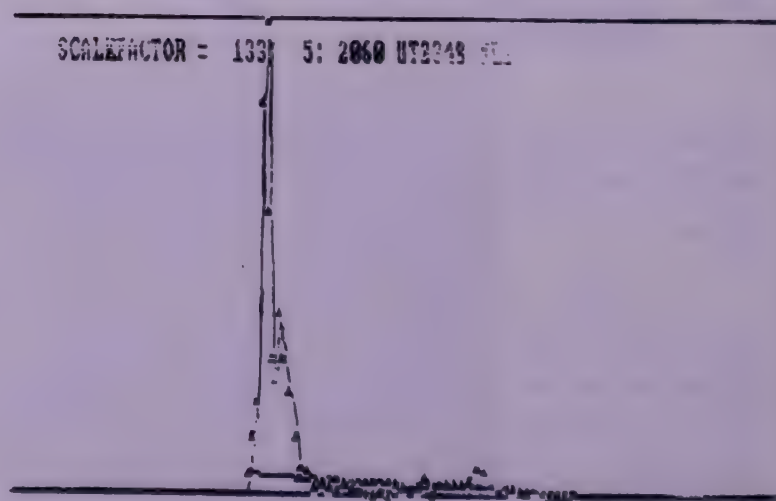
4.7%, S-phase was 9.4% and the DNA index was 1.07.

**Case #2:** This 73-year old black female had three leukoplakic lesions in the left buccal vestibule and left maxillary attached gingiva. She had a long history of snuff use. Microscopic examination of a section from the buccal vestibule revealed hyperparakeratosis with mild epithelial atypia. Section from the attached gingiva exhibited epithelial atrophy, loss of normal rete peg formation, hyperkeratosis, mild epithelial atypia and chronic inflammatory reaction (Fig. 6).

The flow cytometry analysis is illustrated in Figure 7. The G<sub>0</sub>:G<sub>1</sub> was 69.5%, the G<sub>2</sub>:M was less than 1%, the S-phase was 0.3% and the DNA index was 1.10.

**Case #3:** This 65-year old white female presented with a gross calculus, covering her maxillary and mandibular teeth. She had class III periodontitis with enlarged, leukoplakic gingival tissue surrounding the left mandibular premolar teeth. She had a past history of cigarette smoking. The initial biopsy showed epithelial hyperplasia with hyperparakeratosis and marked epithelial dysplasia in the form of hyperchromatic and spindle-shaped nuclei in

the basal-cell layer, variance in the nuclear-cytoplasmic ratio, drop-shaped rete pegs and abnormal mitotic figures (Fig. 8).



*Fig. 5.* Flow cytometry analysis of case 1

Figure 9 depicts the flow cytometry analysis: G<sub>0</sub>:G<sub>1</sub> was 85%, G<sub>2</sub>:M is 5.3%, S-phase was 8.9%, the hyperdiploid shoulder was 8.6%, and the DNA index was 1.08.

A follow-up biopsy of the same area exhibited a frank squamous-cell carcinoma (Fig. 10).



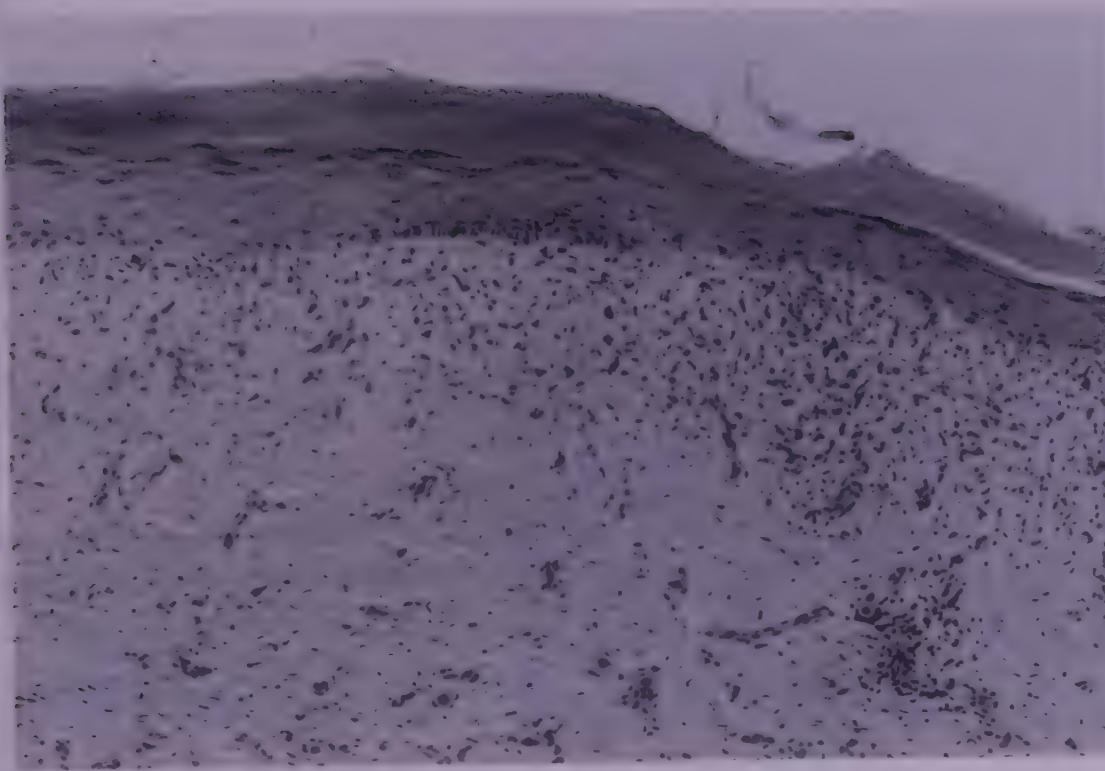


Fig. 6. Epithelial atrophy with loss of normal rete pegs, hyperkeratosis and mild epithelial atypia in case 2

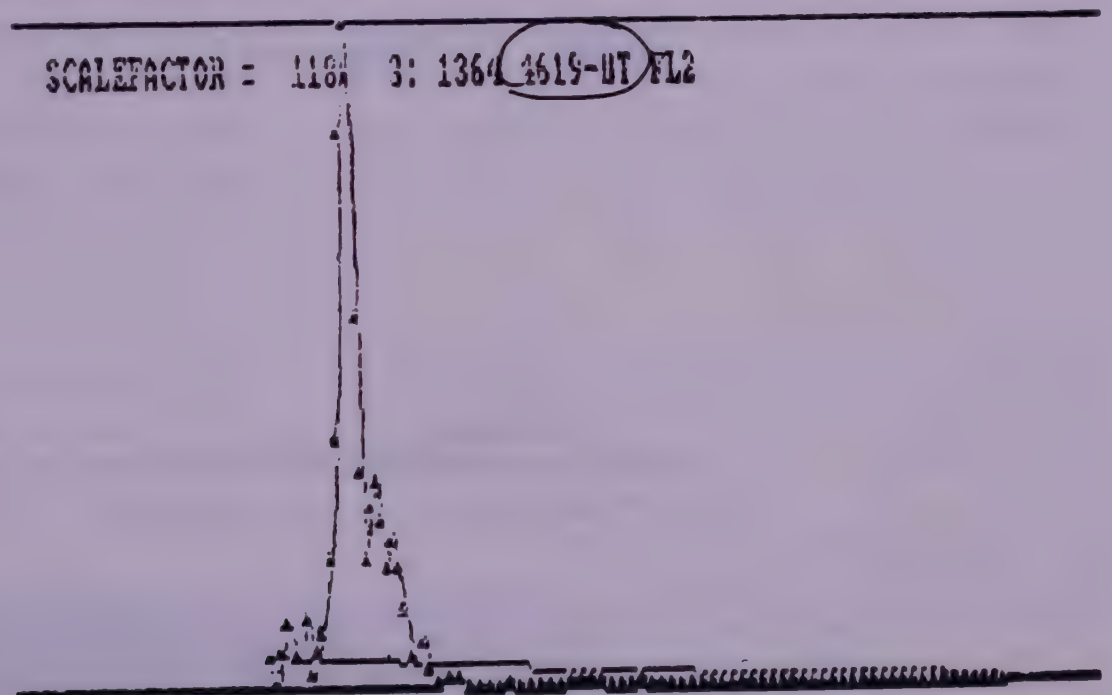


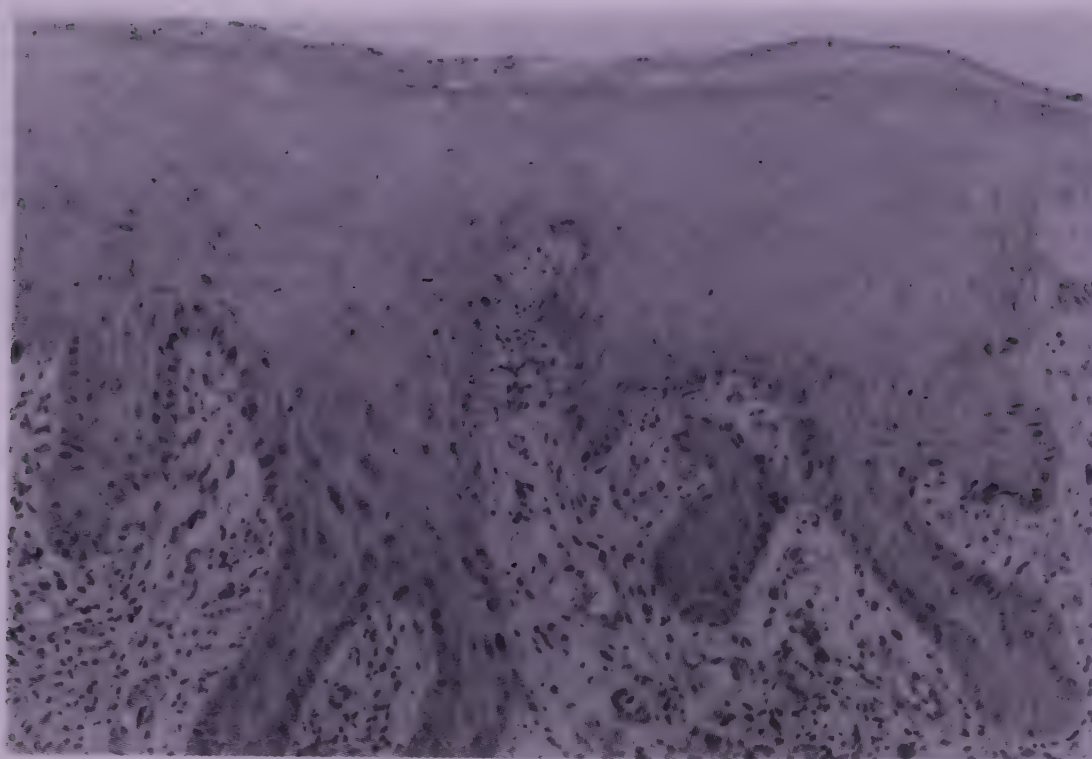
Fig. 7. Flow cytometry analysis of case 2

## DISCUSSION

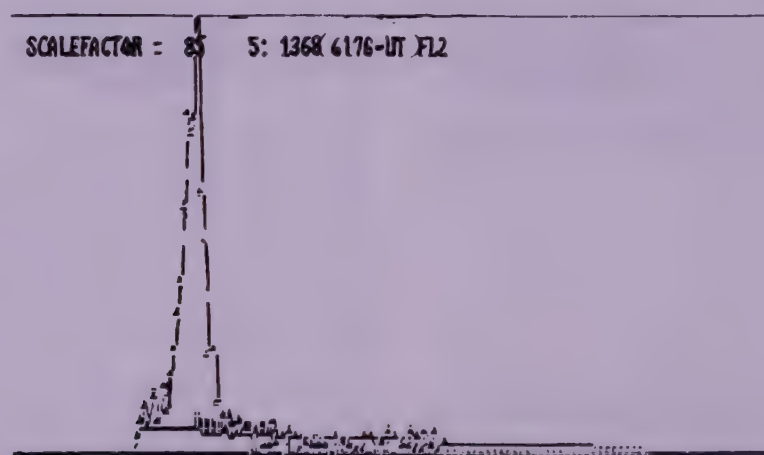
Aneuploid cells are a reflection of genomic instability, which may culminate in cancer.  $G_2$ :M/tetraploid fractions greater than 6% and S-phase cells greater than 7% indicate aneuploidy (or dysplasia), which should be considered suspicious for future malignant change. The normal DNA index is 1.0 (12).

Flow cytometry analysis for case 1 showed a hyperdiploid shoulder with inclusion of 27.4% of the cells. As the normal DNA

should reflect a 1.0 index, this analysis showed a slight increase in DNA among over 27% of the cells. The  $G_2$ :M/tetraploid fraction of 4.7% was within normal limits. The 9.4% S-phase fraction was slightly increased, relative to that in other neoplastic tissues, such as breast cancer. (An increase in breast cancer of a 7% S-phase is considered abnormal.) This pattern suggests an evolving abnormal cell line with a slight increase in metabolic turnover. The patient should be followed closely for any future malignant transformation, even though



*Fig. 8.* Epithelial hyperplasia with parakeratosis and marked epithelial dysplasia in case 3



*Fig. 9.* Flow cytometry analysis of case 3



*Fig. 10.* Squamous-cell carcinoma that developed in case 3



the histopathological appearance is not overly dysplastic.

Case 2 demonstrated a hyperdiploid shoulder with inclusion of 30.2% of the cells. The DNA index was slightly increased, at 1.10; however, the S-phase fraction was very low (0.3%). This pattern suggests an evolving abnormal cell line with low metabolic turnover.

The flow cytometry picture for case 3 showed a predominance of diploid cells with a superficial hyperdiploid shoulder. The percentage of cells in the superficial hyperdiploid shoulder was limited and caused some confusion initially. The S-phase fraction was increased in this tissue (8.9%) relative to the pattern for breast cancer. The G<sub>2</sub>M/tetraploid fraction was borderline, with upper normal limits at 5.3%, and the DNA index was slightly elevated, at 1.08. These factors indicated a very suspicious situation, which was

borne out by the development of oral carcinoma at the same site (Fig. 10). The pattern was suggestive of a very early evolving cell line with a slight increase in metabolic turnover.

These preliminary results from only a few cases indicate that flow cytometry is capable of detecting alterations in DNA content and abnormalities of epithelial proliferation and aneuploidy that are associated with oral epithelial dysplasia and carcinoma. Flow cytometry appears to be a useful adjunct to conventional histopathological examination, and, hopefully, it can be utilized as a predictor of which leukoplakic lesions will progress to cancer.

It is planned to enlarge this study and to utilize fresh surgical tissues from oral leukoplakia and oral cancer to verify the statistical significance of predictability of malignant transformation by flow cytometry.

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# **TOBACCO CONTROL**





# Tobacco control in India: problems and solutions

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Tobacco control is a subject of worldwide importance. India is the third largest producer of tobacco in the world, and the tobacco industry in our country is labour intensive and provides employment to millions of people. It also earns the Government much revenue and foreign exchange. Tobacco in any form, however, is detrimental to health: about 13% of the estimated five million deaths in the adult population can be attributed to tobacco use. A conservative estimate of the annual health care costs attributable to tobacco-related diseases exceeds the revenue earned from tobacco by Rs. 6850 million (US\$ 403 million). The Government of India has initiated several measures to tackle the problem. The Cigarette Act of 1975 stipulates that packets of cigarettes and cigarette advertisements display the statutory warning that cigarette smoking is injurious to health. Laws prohibit smoking in closed spaces such as cinemas, theatres, buses and on domestic flights. Tobacco advertisements are banned in state-controlled media. The National Cancer Control Programme launched in 1984, gave high priority to eliminating tobacco-related cancers. Unfortunately, these measures are yet to make a significant impact. A comprehensive programme is described with the aim of creating a tobacco-free society in the country during the next century.

## INTRODUCTION

Tobacco appears to be as old as human civilization itself. Cultivation of the tobacco plant probably dates back 7000 years: tobacco seeds were discovered in archaeological excavations in Mexico and Peru, and the remains of permanent settlements built around 3500 BC showed that tobacco was an important article to the inhabitants (1).

Documented evidence of tobacco usage has been available since the end of the 15th century. In 1499, Indians on Margarita Island, off the coast of Venezuela, were observed chewing a green herb which was carried in a gourd around their necks. It was assumed that the green herb, known as tobacco, was chewed to quench thirst (2,3). Tobacco chewing appeared to be widespread in the late 1500s in parts of southern America (1); men in Veragua (presently Costa Rica) were also seen to be chewing a dried herb (2). Tobacco smoking

was also popular in the 1500s: Columbus observed American Indians smoking thick bundles of twisted tobacco leaves wrapped in dried palm or maize leaves (4).

Inhaling of powdered tobacco (snuff) seems to have come into vogue much later. Snuff was prepared by grinding tobacco leaves into a powder with a block and pestle of rosewood (5). The Indians of Brazil were perhaps the first to use snuff. In Haiti, it was used as a medicine for cleaning nasal passages and as an analgesic; Mexican Indians were known to have used tobacco powder to heal burns and wounds by the year 1519 (3) and also inhaled powdered tobacco through a hollow Y-shaped piece of cone or pipe called *tobago* or *tobaca* (6).

## TOBACCO PRODUCTION AND USAGE IN INDIA

Tobacco is now cultivated and consumed in various forms all over the world. India is one



of the principal tobacco producing countries, ranking next to China and the USA. Tobacco is cultivated on an area of over 450 000 ha, with an annual production of 450-500 million kg, constituting 7.6% of total world production in 1987. The average yield per hectare increased from 750 kg in 1960-61 to 1199 kg in 1987-88 (7). Increases in the cultivated area, production and yield of tobacco leaf per hectare since 1949 are presented in Table 1. From 1967-68 onwards, the increase in the total area under this crop can be seen to be marginal; total production and average yield per hectare increased by about 2% *per annum*, which is due largely to better cultivation methods. When Indian yield is compared with that in Taiwan (2692 kg), Japan (2468 kg), Australia (2436 kg), Canada (2250 kg), the Republic of Korea (2210 kg), Pakistan (1774 kg) and Burma (1644 kg) (7), it is obvious that our productivity is likely to rise further. This implies increased availability of tobacco in India in the years to come.

**Table 1**

*All-India compound growth rates (%) of area, production and yield of tobacco<sup>a</sup>*

Period	Area ×10 <sup>3</sup>	Production	Yield
1949-64	1.66	2.79	0.96
1967-85	0.05	2.15	2.11
1949-85	0.70	2.16	1.47

<sup>a</sup>Source: ref. (7)

Tobacco is used in various forms in India (see paper by Bhonsle *et al.*, this volume). Although there are no data on the extent of tobacco use on a national basis, reports from different parts of the country show that the prevalence rates vary from 62 to 82% among men and 15 to 67% in women (8). In a study supported by the Indian Council of Medical Research in Goa, 12% of school children were found to be tobacco users (see paper by Vaidya *et al.*, this volume); in Bangalore, Delhi,

Diburgarh, and Ranchi, 56-64% of men over 20 years of age and 14-43% of women were tobacco users.

## TOBACCO ECONOMICS IN INDIA

Tobacco production is a major industry in India. The current gross product value of manufactured tobacco is estimated to be of the order of Rs. 36 000 million (US\$ 2117 million). Twelve companies with 20 factories manufacture cigarettes in India. In 1987, 75 420 million cigarettes, 51% of which were filter-tipped, were produced in India (7). The cigarette industry is capital-intensive in the organized sector, providing direct employment for about 20 000 people and indirect employment for hundreds of thousands of people.

The *bidi* industry, which is essentially a cottage industry, provides gainful employment for more than three million people, mostly in rural areas. Annual production of *bidis* is estimated to be over 550 000 million pieces. Tobacco is used not only for smoking, chewing in various forms (see paper by Bhonsle *et al.*, this volume) and as snuff, but also for making several chemicals (see paper by Chari and Rao, this volume).

The excise revenue earned from tobacco is second only to that from mineral oils, amounting to Rs. 15 515 million (US\$ 916 million) in 1986-87 (7). Tobacco products are an important source of foreign exchange earnings in India: during 1986-87, Rs. 1711 million (US\$ 101 million) were earned through the export of unmanufactured tobacco and of manufactured tobacco products like *bidis*, cigarettes, chewing tobacco, snuff, *zarda* and scented tobacco. Interestingly, India also imports a limited amount of tobacco and tobacco products: in 1984-85, tobacco products worth Rs. 3.8 million (US\$ 22 300) were imported (7).

## NEED FOR TOBACCO CONTROL

In the past, tobacco use was considered by some to be beneficial. In the USA during the



19th and early 20th centuries, dental snuff was used to relieve toothache and neuralgia, to cure bleeding gums and scurvy, to preserve and whiten teeth and to prevent tooth decay (6).

The use of tobacco has, however, been controversial since the beginning. Tobacco was prohibited in Japan in 1590; and taxes on tobacco were increased by 4000% by King James VI of Scotland. In 1633, Sultan Murad IV of Turkey declared that the use of tobacco in any form was a capital offense. During 1613-45, the Czar of Russia prohibited the sale of tobacco. A major attitudinal change towards tobacco chewing arose from the germ theory of infection. In the USA, spitting on the floor and into brass cuspidors was considered a source of contamination and disease spread, and by the 1890s public outcry made tobacco chewing a socially unacceptable behaviour and it became unlawful in most public places (6). Anti-spitting laws were passed in New York and Philadelphia in 1896 and in Toronto, Canada, in 1904 (9).

In India, the earliest observation of the harmful effects of tobacco was made by Niblock (10), who observed in 1902 that cancer of the cheek accounted for almost one-third of all cancer admissions to a general hospital in the State of Madras (presently Tamil Nadu). He attributed this to the tobacco chewing habit, which was prevalent in that region. In 1933, a case-control study indicating a link between tobacco chewing and oral cancer was reported (11). Much later, several epidemiological studies carried out in the Mainpuri district of Uttar Pradesh demonstrated that the earlier the onset of tobacco chewing, the greater the risk for oral cancer (12). The association between tobacco use, oral cancer and precancer was also reported from this area (13-16). The carcinogenic potential of tobacco use has been described in other regions of India as well. For example, in the Bombay area, *bidi* smoking was found to carry risks

for cancers of the oral cavity, pharynx and oesophagus (17,18). A dose-response relationship between smoking and lung cancer in India was also demonstrated (19). Data from the National Cancer Registry Project of the Indian Council of Medical Research (20) showed that 50% of all cancers in men and 20% of those among women are tobacco-related. Furthermore, the annual incidence of tobacco-related cancers was estimated to vary from 20 to 30 per 100 000 men and 12 to 14 per 100 000 women. Although the mortality rates from these cancers are very high, no effective cure is available, but these cancers can be prevented, simply by avoiding the use of tobacco.

It was estimated (21) that if a 20% reduction in the use of tobacco were to be achieved in 1985, as was envisaged, approximately 48 465 cancer cases could be prevented by 2000 AD. In terms of cost economics, the difference between the cost of treating these cancers and the cost of a primary prevention programme, i.e., the net savings, would be around Rs. 265 million (US\$ 15.6 million). Further estimates indicate that the total annual costs for health care (diagnosis and treatment) for tobacco-related diseases (cancers, coronary heart disease and chronic bronchitis) exceed the tobacco revenue by Rs. 6850 millions (US\$ 402.9 million). This is a very conservative estimate, as the cost of establishing essential health care facilities and the loss to the Gross National Product due to tobacco use (disability, fetal loss/underweight) are not included.

Other diseases commonly associated with tobacco use are chronic bronchitis, emphysema, ischaemic heart disease, chronic obstructive pulmonary disease and pulmonary tuberculosis. A cohort study showed that both *bidi* and cigarette smokers had a three-fold greater risk of developing coronary heart disease or myocardial infarct than nonsmokers (22).

The harmful effects of tobacco also include increased risk of low birthweight,



spontaneous abortion, stillbirth and neonatal deaths. An excess rate of stillbirths was observed among smokers (50 per 1000 births) compared to nonsmokers (17 per 1000 births), and babies born to mothers who smoked weighed on average 100-200 g less than babies born to mothers who did not smoke (23). In another study (24), children born to mothers who smoked weighed an average of 395 g less than those born to nonsmoking mothers (see paper by Krishnamurthy, this volume).

Numerous biochemical investigations on tobacco products also confirmed their harmful nature. For example, carcinogenic and cocarcinogenic polycyclic aromatic hydrocarbons were found in substantial amounts in *mishri*, which is applied to the teeth and gums, and in snuff used for inhalation (25). Nicotine, carbon monoxide, hydrogen cyanide, volatile phenols, polycyclic aromatic hydrocarbons, acrolein and acetaldehyde contribute to the toxicity/carcinogenicity of tobacco smoke (26). Betel quid also contains several carcinogenic substances (see paper by Hoffmann *et al.*, on smokeless tobacco, this volume). These findings indicate unequivocally that tobacco consumption in any form is a substantial health hazard.

It is estimated that at least 630 000 deaths among people aged 15 years and above in India are directly attributable to tobacco use; this forms 23% of the total deaths among men and 4% among women (8).

The tobacco industry spends Rs. 2682 (US\$ 102) per ha, amounting to Rs. 1200 millions (US\$ 70.6 million) *per annum* in curing the tobacco. The major share of this, which is on fuel, is Rs. 1598 (US\$ 94) per ha, totalling Rs. 703 million (US\$ 41.3 million) *per annum* (7). These figures indicate that since the tobacco industry requires considerable energy resources for curing, it is also responsible to some extent for deforestation in the country, which will lead to ecological imbalance in the years to come.

## PROBLEMS AND POSSIBLE SOLUTIONS FOR TOBACCO CONTROL

Possible tobacco control measures can be split broadly into (i) sociobehavioural aspects; (ii) pharmacological and psychological aspects; (iii) economic losses and gains; and (iv) political will.

**Sociobehavioural aspects:** Every effort should be made to make tobacco use an antisocial habit, be it at home, at work, in public places or at social gatherings. Some state governments in India — for example, those of West Bengal, Tamil Nadu, Kerala, Karnataka, Maharashtra and Gujarat — have promulgated laws prohibiting smoking in enclosed areas, such as cinemas, buses, educational institutes and hospitals. Smoking is prohibited currently on all domestic flights of Indian Airlines. Any advertisement or even mention of tobacco is banned on the broadcasts of All-India Radio.

To achieve the aim of a tobacco-free society, environmental situations must be created in which nonsmokers are given preference over smokers. In order to achieve this, many gradual and carefully designed steps will have to be undertaken. For instance, antitobacco education, focused on young nonusers through an extensive, persuasive campaign would be an important step in that direction. Use of the mass media, voluntary agencies, women's organizations, educational institutions, religious organizations, shrines, no-tobacco days for users and traders, and messages from health-related institutions should be explored. Periodic cross-sectional assessment to measure the impact of such educational programmes would be essential in order to make the mid-course corrections.

**Pharmacological and psychological aspects:** Termination of nicotine ingestion, even after intake of small quantities (daily dose, 0.002 mg/kg body weight), produced behavioural patterns associated with aggressiveness,



hostility and irritability (28). Thus, nicotine acts as a reinforcing agent in tobacco smoking. The nicotine withdrawal syndrome, which includes sleep disturbances, changes in brain wave-pattern, fall in pulse rate and blood pressure, anxiety, nervousness and fatigue, contributes to the difficulty in giving up tobacco.

Counselling centres for quitting the tobacco habit, comprising psychological support to tobacco users, would be necessary. In some situations, the focus could be on mitigation rather than on elimination. People continue to smoke because of dependency due to cognitive helplessness: research must therefore be undertaken to find ways to satisfy their psychological and pharmacological needs. Non-smokers' rights in the face of the dangers of passive smoking are another important social issue. In a large proportion of people, initiation into alcohol and drug abuse starts after tobacco use (28).

**Economic aspects:** As discussed above, tobacco contributes to both the negative and positive aspects of the country's economy, but the losses to the economy far outweigh the gains. Unfortunately, this fact is still not well known and should be proven with sound data. While the gains are clear, in the form of employment generated by tobacco-related activities and revenue and foreign exchange earnings, the losses occur in the form of costs incurred in providing health care for people with tobacco-related diseases due to loss of productivity caused by decreased efficiency, disability and premature death. The use of wood in tobacco curing, resulting in environmental degradation and soil erosion, also has serious economic implications.

A conservative estimate, based on the impressions of a number of clinicians, of the cost of treatment of three major tobacco-related diseases, namely, cancers, heart diseases and bronchitis, is that it costs the government about Rs. 24 190 million (US\$ 1422.8 million) annually, which is Rs. 6850 million

(US\$ 402.9 million) more than the revenue and foreign exchange provided by tobacco to the Government. As mentioned earlier, these estimates do not include the cost of diagnosis and treatment of other diseases and disorders or the cost of establishing health care facilities such as radiotherapy units and computerized tomography scanners.

Experience all over the world has shown that a gradual price rise is an effective means of reducing the smoking habit. Thus, a gradual increase in the prices of all tobacco products in the country would be the right approach.

**Political will:** A necessary ingredient for the success of any national programme is political and administrative support. Politicians and administrators must be convinced of the magnitude of tobacco-related problems, so that they will promulgate and strictly enforce any legislation directed towards tobacco control. Politicians can also act as leaders for anti-tobacco programmes, and this increases their chances of success. The political will can be stimulated by close interaction between scientists (health, agriculture, industry), politicians and administrators.

## EFFORTS OF THE GOVERNMENT OF INDIA TOWARDS TOBACCO CONTROL

Realizing the magnitude of health problems associated with tobacco usage, the Government promulgated The Cigarette Act, 1975 (regulation of production, supply and distribution), which requires that all manufacturers or persons trading in cigarettes display prominently a statutory warning, 'Cigarette smoking is injurious to health', on all cartons and packets of cigarettes that are put on sale. This, however, made no significant dent in the smoking habit; because (i) the statutory warning is limited to cigarettes, which are consumed much less than *bidis*, which are cheaper and more harmful; and (ii) the printed warning can be read only by literates.



It has been suggested that, in view of the diverse forms of tobacco use, (i) the statutory warning be extended to other tobacco products; (ii) the warning be printed in local languages; and (iii) the warning made more effective by a pictorial depiction, for instance, in the form of a skull-and-crossed-bones. The printing of more direct messages like 'Tobacco can cause cancers and heart diseases' in local languages might also be useful. Printing the tar and nicotine levels on packets and cartons of all tobacco products and fixing the maximum permissible limits of these toxins for all tobacco products should also be made mandatory. High levels of taxation should be placed on high-tar, high-nicotine tobacco products. Both cigarettes and *bidis* should be required by law to have effective filters.

On the recommendations of the Luthra-Bisht Committee in 1984, a national cancer control programme was formulated, which gave impetus to the antitobacco cause. Noting that tobacco-related cancers account for about one-third of all cancers in the country, primary prevention of tobacco-related cancers constituted a major objective of this programme. Accordingly, the National Cancer Control Board and state cancer control boards have given high priority to antitobacco educational programmes for primary prevention of tobacco-related cancers. To date, 17 states and union territories in the country have constituted such cancer control boards.

Monitoring and controlling scenes that glamourize smoking in films, Doordarshan (television) programmes and road-side advertisements constitute another important control measure. As described earlier, a complete ban on tobacco advertisements in government media exists, and smoking is prohibited on domestic flights.

It is realized, however, that such governmental steps, although commendable, are not sufficient to make an impressionable dent on the tobacco habit of the community: it is

necessary to have a comprehensive programme for tobacco control. The main planks of such a comprehensive programme should comprise tougher antitobacco legislation, a gradual price rise on tobacco, changes in agricultural practices to replace tobacco by other crops, finding alternative uses of tobacco, modifying tobacco products to make them less harmful and an aggressive health education campaign to wean people away from tobacco. Other steps that the Government should initiate urgently are: protection of nonsmokers in public places from passive smoking; banning tobacco advertisements in all public places; making it unlawful to sell tobacco items to people below the age of 18; sale of cigarettes and *bidis* in packets, as opposed to selling them singly; prohibition of the sale of tobacco in and around educational, health and religious institutions; and a ban on tobacco imports.

## OPERATIONAL RESEARCH ON AN ANTITOBACCO PROGRAMME

The experience all over the world is that antitobacco education is an effective means of stopping or curtailing tobacco use. Although such efforts have to be targeted at users as well as nonusers of tobacco, the most profitable target group is the young nonuser. An intervention study by the Tata Institute of Fundamental Research, Bombay, showed that 9-17% of people stopped tobacco use and 20-49% reduced their habit substantially after five years of health education (27). The Indian Council of Medical Research initiated a multicentre study in Bangalore, Goa, Agra and Trivandrum, utilizing the existing health infrastructure. Workers at the Goa centre are also studying the use of school children as a means of changing tobacco habits in a community.

All-India Radio, in collaboration with the Indian Council of Medical Research, will soon initiate an educational programme on the hazards of tobacco, drugs and alcohol. This programme (Radio Date) will be broadcast in 17



regional languages, as a weekly serial with 28 episodes, by all of the 104 broadcasting stations, focusing on the rural community aged 10 years and over.

## RESEARCH PRIORITIES

Operational research for antitobacco community education must be strengthened, and various agencies can be used for this purpose. A single approach will not be suitable for all population groups, but packages for different areas of the country could be devised and implemented. Research on tobacco usage would

help in deciding the most effective method of community-based intervention.

A major hindrance to implementing anti-tobacco legislations is the fear of loss of employment and the revenue earned from tobacco. As described above, however, the amount spent on the treatment of tobacco-related diseases outweighs the gains due to tobacco revenue and export. The Indian Council of Medical Research is initiating studies on the cost of managing tobacco-related diseases, which will help in computing the tobacco economics for the country more accurately.

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# Control strategies for tobacco-related cancers in Kerala, India

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Various cancer control activities undertaken by the Regional Cancer Centre, Trivandrum, Kerala, India, include a novel method of utilizing the services of National Service Scheme volunteers, primary health care workers, social workers and unemployed youth in both primary and secondary prevention of cancer. These approaches were found to be effective.

## INTRODUCTION

Cancer control implies a broad spectrum of activities aimed at primary prevention, reduction in morbidity and mortality and rehabilitation. The basis for cancer control is research in basic sciences, cancer epidemiology, diagnostics, clinical oncology, social sciences, rehabilitation, health care organization and health delivery. Many countries have formulated cancer control policies consistent with their needs and priorities (1), and India is one of them (2). Tobacco-related cancers constitute 50-55% of cancers among men and 20-25% among women in India (3,4). Accordingly, in the National Cancer Control plan, primary prevention formed an important objective. In consonance with this objective, the State of Kerala on the south-western coast of India has formulated its own cancer control programmes (5). This paper gives an overview of the activities conducted by the Regional Cancer Centre (RCC), which is a major cancer treatment centre in the State.

## CANCER IN KERALA

Data from the RCC show that every year 15 000 new cancer cases occur in the State (4). Of these, 17% among men and 11% among women are oral cancers. Other common

cancers among men include cancers of the lung (11.5%), oesophagus (5.8%) and larynx and pharynx together (7%). Among women, the common cancers include those of the uterine cervix (25%) and breast (17%).

## CONTROL STRATEGIES IN KERALA

To facilitate the planning of control strategies, the following data were collected: (i) the pattern of tobacco usage in the community; (ii) knowledge, attitude and perception of the general population; (iii) referral pattern; (iv) incidence rates of various cancers; (v) clinical extent of cancer at first presentation; and (vi) proportion of cases receiving radical treatment.

Several measures are being implemented in the State, but the major emphasis is on primary prevention, with an interdisciplinary approach utilizing health care delivery agencies and voluntary organizations. The various activities can be summarized as follows: Primary prevention involves surveys of tobacco use and of knowledge, attitude and perception, cancer registration, health education, tobacco cessation clinics, chemoprevention and legislation. Secondary prevention consists of utilization of primary health



workers, volunteers to the National Service Scheme and unemployed youth, cancer detection camps and peripheral centres for early detection of cancer. Tertiary prevention involves therapeutic intervention, surgical reconstruction, clinical trials, pain clinics and psychosocial surveys of morbidity.

### **Primary prevention:**

**Tobacco surveys:** Information on the prevalence of tobacco use is important for planning control measures and was obtained from different parts of the State. For example, 13 000 people in the south were interviewed by health and social workers. These individuals represented a 10% sample of the 278 census enumeration blocks in each of which the entire population was enumerated for tobacco habits. In central Kerala, unemployed youth collected this information from 11 420 people; in Kottayam, all individuals over the age of 21 were screened by National Service Scheme volunteers with regard to their tobacco habits and alcohol consumption, as part of an oral cancer screening programme.

Tobacco smoking by itself or with chewing was common (46%) among men; only 9% were exclusively chewers. An overwhelming proportion (92%) of women in this group did not use tobacco. Compared to data available from other sources, these prevalences are rather different. Information on alcohol consumption was also collected from these individuals.

**Surveys of knowledge, attitude and perception:** Table 1 summarizes information collected on knowledge, awareness and perception about cancer among 600 individuals by hospital social workers. A high level of awareness was observed about cancer in general, about warning signals and about the risk factors for oral cancer. The knowledge of medical students was monitored in another survey, and such information is now being obtained from physicians and surgeons.

**Table 1**

*Awareness about cancer among 600 individuals in Kerala*

Criteria	Percent
Heard about cancer	100
Aware about at least one or more risk factors for oral cancer	67
Aware about at least one or more risk factors for lung cancer	28
Aware about at least one or more of the seven warning signals of cancer	75
Aware about at least one or more common cancers	65

**Cancer registration:** Since 1982, a hospital-based cancer registry has been functioning at the RCC, which is the only cancer treatment centre in southern Kerala. Data from this source is used to compute the minimal incidence rates of different cancers in order to study their trends. Information on referral practices, the clinical extent of cancers at presentation, treatment modalities and prognosis is also available from the registry.

**Health education:** Helping people to avoid tobacco use is accorded high priority in the cancer control programme. With that view, various health educational programmes are being undertaken at the Community Oncology Centre of the RCC. Electronics and the press are being used to disseminate information about tobacco related-cancers to the public. Further, audiovisual programmes on cancer are being shown during cancer detection camps in various parts of the state. School children will be educated on the harmful effects of tobacco and will be used later to spread the messages. Suitable material to be included in the school curriculum is being developed. As part of self-help measures, pamphlets on examining one's own mouth are distributed periodically, so that they will reach a large number of households. The various health education measures thus comprise (i) school-based intervention, (ii) self-help strategies, (iii) mass media approaches, (iv) community-based



intervention and (v) intervention specially directed to high-risk populations.

*Tobacco cessation clinics:* Quitting the use of tobacco is complex and requires continuous support from various sources. Thus, tobacco cessation programmes should include health education, motivation and psychological, social, family and sometimes pharmacological support in order to bring attitudinal changes and modification of behaviour. Implementation of these programmes, therefore, must be multidisciplinary, involving clinicians, psychologists, sociologists and family support in a suitable environment. We envisage conducting tobacco cessation clinics incorporating the necessary infrastructure, especially for heavy tobacco users. The reasons for the high level of health awareness among some individuals may be applicable for primary prevention in others. We will therefore collect this information from a sample of the 100 000 individuals who registered themselves in the Kerala government scheme 'Cancer care for life'.

*Chemoprevention:* Chemoprevention is a major experimental activity for the control of oral cancer and precancer at the RCC, which is being conducted in collaboration with the British Columbia Cancer Research Centre, Vancouver, Canada. The main objective is to determine whether micronutrients can lower the risk of cancer by preventing or reverting the process of carcinogenesis. The feasibility of using micronucleated cells as intermediate endpoints is being evaluated.  $\beta$ -carotene and vitamin A intake appear to result in higher rates of regression of leukoplakia among heavy chewers, smokers and alcohol users (6-8). The optimal doses, spacing and maintenance of these vitamins were also determined. Chemopreventive agents are believed to act even with the continued action of etiological factors; however, whether these agents really reduce the risk for cancer is yet to be determined from long-term follow-up studies. At this stage, the emphasis is on clinical trial; we hope to translate the experiences gained from these studies

into a full-scale chemopreventive intervention trial.

### **Secondary prevention:**

*Use of primary health workers for early detection of oral cancer:* Studies conducted in Sri Lanka (9) and in the Ernakulam district of Kerala (10) demonstrated that primary health care workers can be used in oral cancer detection programmes. A similar study is in progress in the northern part of Trivandrum district: primary health care workers in six primary health centres were trained by the RCC to identify people at risk and to examine their mouths to detect oral cancer and precancerous lesions. An area covered by primary health care workers in the southern part of the Trivandrum district has been selected as the control area. It is proposed to compare the numbers of oral cancer cases arriving from these two areas to evaluate whether early detection has been achieved in the study area.

*Use of unemployed youths for early detection of cancers:* Some 92 unemployed youths belonging to a community of 14 000 persons were informed about the seven warning signals of cancer and were briefly trained to examine the oral cavities of high-risk persons. These youths then screened 13 959 people from that community and identified 397 high-risk individuals. While examining the individuals, they also disseminated information on the seven warning signals. People who thought they might have cancer on the basis of these signals and people found by the unemployed youths to have a suspicious oral lesion were advised to consult physicians. Employing this method, nine cancers, of which four were buccal cancers, and 169 precancerous lesions and conditions were detected, vindicating the feasibility of using such young persons in oral cancer detection programmes.

*Use of National Service Scheme volunteers:* The National Service Scheme is a voluntary student organization which is involved in various



developmental programmes in the community. The organization has different levels of leadership and implements many socially relevant schemes, such as teaching, hygiene and immunization, in the community. For the present purpose, volunteers were instructed about the seven warning signals of cancer and were also trained to conduct oral examinations. They have screened 4041 persons so far, and detected 15 oral cancers; 12 in clinical stages 1 and 2 and three in stages 3 and 4; they also found 92 precancerous lesions and conditions, which were confirmed by physicians. Thus, the strategy of using National Service Scheme volunteers was found to be fruitful, and they are now being used regularly in screening programmes in Kottayam.

*Early detection centres and cancer detection campaigns:* Two peripheral centres for early detection of cancer were established in Ernakulam and Palghat by the RCC in collaboration with the Kerala State Health Services Department. The main purpose of these peripheral units is to provide diagnostic services for cancers of the head and neck, breast and uterine cervix (11). The units also organize regular cancer detection campaigns in the community in order to examine high-risk individuals and to follow-up cases of precancer.

#### ***Tertiary prevention:***

Tertiary prevention encompasses reconstruction, rehabilitation and pain control therapy. In order to provide optimal treatment and minimal loss of structure, a combined approach consisting of surgery, radiation and chemotherapy is used for treating cancer at the RCC. Regular programmes propagate this approach to other centres in Kerala.

Clinical trials to assess the efficacy of multi-modal treatment of advanced tobacco-related cancers are in progress at the RCC. The cancer surgery division uses an indigenous reconstruction technique for oral and head-and-neck cancers. Pain relief management consistent with that recommended by the WHO global programme on cancer pain relief is part of the treatment protocol at the RCC, and this knowledge is disseminated to other centres in the State. Objective and subjective assessments of various pain relief methods are also being planned. Psychosocial surveys on morbidity of cancers of the head-and-neck, breast and cervix are being contemplated.

#### **DISCUSSION**

Kerala is a small state with a high literacy rate (65%), which is advantageous for raising the health consciousness of the people. As elsewhere in the country, tobacco use is deeply entrenched. In order to combat its health consequences, the RCC, in association with medical colleges in the State, the Health Services Department of Kerala Government, National Service Scheme volunteers, unemployed youth, general practitioners and various social organizations, has embarked on multifaceted cancer control activities. The active concern of the Government regarding the health consequences related to tobacco use and its supportive action are encouraging. For instance, the Government is contemplating measures to prevent tobacco from being available to children and to deter tobacco use in public places, educational institutions and Government offices. It is hoped that these attempts will produce the desired results in the near future.

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# Achieving smoking cessation in healthy and cancer patient populations through the use of self-help materials and physician advice

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Self-help smoking cessation materials can be used for a variety of target populations by virtue of special language, cultural and other types of tailoring, and can also be combined with more intensive intervention components as desired. Large numbers of people can be reached, and materials can be distributed using the mail system or personal contact. In Los Angeles, we have developed a number of different self-help programmes for registered nurses, pregnant women, patients with newly diagnosed squamous-cell carcinomas of the head-and-neck, and women members of a pre-paid health plan who were not volunteering to stop smoking. Our experiments with the self-help format have shown promise in terms of the outcome evaluations. Results for the study involving registered nurses showed approximately a 20% quit rate at one-year follow-up. Other studies have just been completed or are in progress.

## INTRODUCTION

Over the past 20-30 years, a vast body of experience has been accumulated with a variety of approaches for helping people to stop smoking. These include: (i) group or clinic programmes, usually with an educational and/or behavioural modification approach; (ii) individual treatment, which might feature psychotherapy, behavioural modification or hypnosis; (iii) health care provider interventions, with routine counselling and/or more intensive methods; (iv) information disseminated by the mass media; (v) pharmacological agents, including nicotine chewing gum and other prescription medications and; (vi) self-help approaches (1,2). The latter encompass a variety of books, manuals and other types of aids to quitting, which might include audio- and videotapes, hand-held computers, non-prescription medications and filters and cigarette substitutes.

In the USA, survey data have shown that most persons prefer to stop smoking on their own without formal assistance or programme attendance, and that over 90% of successful ex-smokers stopped by themselves (3-5). The median quit rates for self-help programmes are approximately 14-20% after one year, which is somewhat lower than for group or intensive treatment programmes (1,3). However, given the preference of smokers for self-quitting and the estimated number of adult smokers in the US population today (40 million), the appeal of self-help programmes is great from a public health perspective. Glynn *et al.* (6) summarized the essential elements of self-help/minimal intervention strategies for smoking cessation. The public health approach focuses on all smokers, seeks to establish a cultural norm of nonsmoking with a long-term and sustained time frame, proposes to utilize a range of intervention options from



which people can select, and is evaluated *via* temporal changes in the population prevalence of smoking.

One of the great appeals of self-help smoking cessation materials is that they can be used for a variety of target populations by virtue of special language, cultural and other types of tailoring and can be combined with more intensive intervention components, as needed. Large numbers of people can be reached, and the materials can be distributed using the mail system or personal contact. Table 1 shows the recommendations from a consensus document for essential elements of self-help/minimal intervention strategies.

**Table 1**

*Essential elements of self-help/minimal intervention strategies of smoking cessation<sup>a</sup>*

- 
- |    |   |    |  |    |   |
|----|---|----|--|----|---|
| 1. | Intervention efforts should focus on increasing smokers' motivations to make serious attempts to quit   |    |  |    |   |
| 2. | Delivery of programmes be broadened to include all smokers  |    |  |    |   |
| 3. | Programmes be targeted to stages of cessation and specific populations  |    |  |    |   |
| 4. | All programmes include: <table border="0" style="margin-left: 20px;"> <tr> <td style="vertical-align: top; padding-right: 10px;">a.</td> <td>elements focused on health and social consequences of smoking, and</td> </tr> <tr> <td style="vertical-align: top; padding-right: 10px;">b.</td> <td>strategies and exercises aimed at quitting, maintenance of nonsmoking, relapse prevention and recycling</td> </tr> </table> | a. | elements focused on health and social consequences of smoking, and | b. | strategies and exercises aimed at quitting, maintenance of nonsmoking, relapse prevention and recycling |
| a. | elements focused on health and social consequences of smoking, and  |    |  |    |   |
| b. | strategies and exercises aimed at quitting, maintenance of nonsmoking, relapse prevention and recycling   |    |  |    |   |
| 5. | Materials and programmes be made widely available rather than 'fine tuning' existing programmes or developing new ones  |    |  |    |   |
| 6. | Programmes make use of specific adjunctive strategies   |    |  |    |   |
- 

<sup>a</sup>Source: ref. (6)

In Los Angeles, we have studied the process of unaided smoking cessation and have also developed and tested self-help programmes for various populations, such as registered nurses, women members of a pre-paid health plan who were not volunteering to stop smoking, patients with newly diagnosed

squamous-cell carcinomas of the head-and-neck, and persons from racial/ethnic minority groups, many of whom are socioeconomically disadvantaged. In each of these self-help programmes, the written materials contained the same core of information necessary to stop smoking and remain abstinent. Additionally, special portions of the contents and the style in which the materials were written addressed the salient needs and concerns of each target population; the level of literacy assumed varied according to the population.

The self-help programmes further differed in terms of the components that supplemented the written materials. The two extremes encompassed a series of six booklets mailed to women health plan members at home with no personal intervention, and personalized cessation counselling given by doctors or dentists, accompanied by the materials, contracts for date of quitting, reminder postcards and further booster sessions of counselling by health care providers over a six-month period.

Our experiments with the self-help format have shown promise in terms of outcome, comparable to published data from a variety of unaided and self-help trials, which showed median one-year point prevalence cessation rates of 14-20% (1,3). Results have been published from our study of unaided smoking cessation and from the study involving registered nurses; other studies have just been completed or are in progress.

The remainder of this paper reviews the research and findings in self-help smoking cessation that was undertaken by the UCLA Division of Cancer Control and discusses advantages as well as potential problems and disadvantages. Table 2 summarizes comparative data for the various study samples.

## UNAIDED SMOKING CESSATION

As part of our research on self-quitting, we conducted a study of 554 people who had set either the 'Great American Smokeout' or 'New



**Table 2***Summary of the results of UCLA unaided and self-help smoking cessation studies: description of study samples and outcomes*

	Study sample (means or percents)			
	Unaided (n=554)	Nurses (n=149)	Health maintenance organization members (1396)	Head-and-neck cancer patients (n=109)
<b>Demographics</b>				
Age (years)	41.4	37.7	38.4	57.3
Sex				
Male	44%	6%	0%	71.6%
Female	56%	94%	100%	28.4%
<b>Smoking history/dosage</b>				
Cigarettes per day				
Current	22.7	19.6	19.2	23.4
Heaviest	33.2	— <sup>+</sup>	— <sup>+</sup>	33.1
Years smoked	22.8	19.3	19.3	39.0
Fagerstrom tolerance scale	5.8	4.9	— <sup>+</sup>	— <sup>+</sup>
Self-reported addiction (5-point scale)	4.5	4.4	4.4	4.3
Desire to quit (5-point scale)	4.6	3.2 (4-point scale)	3.7	4.2
Confidence in remaining abstinent (5-point scale)	3.8	2.8 (4-point scale)	2.4	4.0 (current) 4.8 (former)
<b>Outcome — 12 months</b>				
Ever quit	79%	57%	54.4%	—*
Point-prevalence quit	25%	19.5%	15.2%	—*
Continuous abstinence	11%	12.7%	4.2%	—*

<sup>+</sup>Question not asked

\*Study in progress; data not available

Year's Day' as target dates for permanent cessation and who intended to quit without formalized external aid (7). The 'Smokeout' is an annual 24 h, nationwide quitting event which is sponsored by the American Cancer Society, and 'New Year's Day' is a popular time for Americans to 'resolve' to give up bad habits. We enrolled all subjects prior to their target quit date and then interviewed them periodically by telephone for one year. Reports of smoking abstinence were checked with confederates — persons whose name and telephone number were supplied by subjects; 92% of

reports of abstinence were confirmed, 2% were disputed, and 6% were unknown.

The mean age of the cohort was  $41.4 \pm 13.5$  years, and 44% were male. Our subjects smoked a mean of  $22.7 \pm 11.1$  cigarettes per day and were slightly heavier smokers than the general population. On a five-point scale, their self-reported level of addiction was  $4.5 \pm 1.0$ . The mean Fagerstrom tolerance score was  $5.8 \pm 2.1$  on an 11-point scale (8). What was very impressive about these subjects was their motivation to quit, their self-confidence in their ability (self-efficacy) and their readiness



(stage of change). On a five-point scale (1=not at all; 5=very much), the mean level of motivation was  $4.6 \pm 0.6$ , the mean level of confidence about stopping was  $3.7 \pm 1.0$ , and the mean level of confidence about staying off was  $3.8 \pm 1.0$ . Furthermore, according to the stages of change model of Prochaska and DiClemente (9), all subjects were in the contemplation stage; 58% were 'contemplators-ready-for-action', having made an effort to quit in the preceding year.

The results from this study are extraordinary and, in fact, comprised the highest quitting rates reported in 10 prospective trials of self-quitting in the overview given by Cohen *et al.* (3). The point-prevalence smoking cessation rate at one year was 25.1%, and the continuous abstinence rate was 10.6%. Overall, 79% of the subjects succeeded in quitting for 48 h or longer, although 68% of these had relapsed by the end of the year. Continuous abstainers were lighter smokers, less addicted, more aware of the health risks associated with smoking, more highly motivated to stop, more confident of their ability to do so, and more committed to quitting than other subjects. While many of these descriptors of the most successful subjects are those commonly identified from formal treatment programmes (10-12), the key element may be the stage of change variable.

### SMOKING CESSATION BY REGISTERED NURSES

The first population for which we chose to design a tailored self-help smoking cessation programme was registered nurses, health professionals with a notoriously high smoking prevalence in 1976 (39%, compared to 25% for physicians, dentists and pharmacists) (13). By 1985, the prevalence among the nurses had declined to 23% (14), but concern still remained with regard to the teaching, exemplar and role model functions of nurses, the even lower smoking rates of physicians (10% or less), and the continuation of nurses'

smoking in health care settings amid circumstances that logically mitigate against it.

Thus we selected registered nurses because of their high-risk smoking profile, their predominantly female membership, the social convention that seemed to support their continued smoking and their complex work environments. The self-help intervention had two components — printed manuals and a supportive environment at work (15). We selected the American Lung Association cessation manuals — 'Freedom From Smoking (quitting)' and 'A Lifetime of Freedom From Smoking (maintenance)' — which were considered the best. We also held focus groups and developed three specialized manuals based on the most prominent concerns of nurses about stopping smoking: taking a break at work, utilizing social support (buddies), and managing weight. The four-month worksite component of the intervention consisted of buttons with the programme logo, 'Make the Break', posters, newsletters and a 'Great Nurses Smokeout Day' event. The latter was timed to correspond to the target date for quitting in the manual and featured a booth set up in the cafeteria at which carbon monoxide testing in breath, a videotape of women discussing quitting smoking and additional written information were available.

We recruited 164 registered nurses and 48 other staff at 15 hospitals in the greater Los Angeles area which represented 58% of those who initially returned the recruitment flyer. After dropping late enrollees, we were left with a sample size of 149. All nurses received the intervention, and we utilized an uncontrolled, pre-test/post-test design.

Enrollment meetings were scheduled at each hospital at (multiple) times convenient for nurses who were working with a variety of schedules. Each nurse filled out a base-line questionnaire and received the printed materials and buttons. Thereafter, nurses were followed by telephone interview for one year.



Worksite visits were scheduled to collect saliva samples in order to validate smoking abstinence (92% agreement). This population would be extremely difficult to approach within group programmes, given the diversity of work circumstances in hospital settings.

As with our unaided sample, enrollees constituted a higher proportion of heavier smokers than the general population; they smoked a mean of  $19.6 \pm 9.7$  cigarettes per day, had a self-reported addiction of cigarettes of  $4.4 \pm 0.9$ , and a Fagerstrom tolerance scale score of  $4.9 \pm 1.9$ . On four-point scales, motivation to quit was  $3.2 \pm 0.7$ , self-confidence in quitting was  $2.8 \pm 0.8$  and confidence about maintaining abstinence was  $2.8 \pm 0.9$ . Their mean age was  $37.7 \pm 8.4$ , and 94% were female.

Results showed that 57% of subjects had quit for 48 h or longer and 75.3% of these had relapsed by the end of the year. At 12 months, the point-prevalence abstinence rate was 19.5%, and the continuous abstinence rate was 12.7% — both very respectable by self-help standards (3). Predictors of 12-month point-prevalence abstinence included daily consumption (negative), use of the American Lung Association maintenance manual and two attitude items related to nursing (stress arising from working with dying patients and stress arising from physician opposition to upgrading nursing service (negative)). It is interesting that only 52% of the nurses reported using the cessation manual, 20% the maintenance manual and 22-25% each of the three specialized manuals. Nurses who did use the materials rated them positively, 63-95% responding 'very' or 'somewhat' helpful. Thus, programme enrollment, even by volunteers, guarantees neither a serious attempt to quit nor use of programme materials, no matter how well they are tailored to participants' needs.

The results of this study are quite promising, and the programme was turned over to the American Cancer Society and presented in a

number of workshops (15). Unfortunately, a controlled evaluation proved unfeasible, and we cannot make further assumptions about the efficacy of the programme.

### **SMOKING CESSATION IN FEMALE MEMBERS OF A HEALTH MAINTENANCE ORGANIZATION**

We have recently completed a study of targeted self-help materials designed for a non-volunteer population of women (16), all of whom are members of a large southern California health maintenance organization, a prepaid type of health care plan. This study again, focused on women, but we were interested in the public health issue of whether unsolicited smoking cessation materials would produce a shift in the population prevalence of smoking in a group probably composed of a much higher percentage of precontemplators than the usual volunteer sample. This study presaged the consensus recommendations, as well.

We enrolled 1410 women who were daily smokers in this 'UCLA Preventive Health Behaviour Study', in which they agreed to be interviewed periodically by telephone over an 18-month period about a variety of preventive health behaviours, including diet, exercise, seat belt use, alcohol consumption, stress and smoking. These subjects were identified through a routine needs' assessment telephone interview of 15 004 female members of the health plan. Twenty percent were smokers, who were invited to participate in the study, although they were unaware of this selection factor. Less than half of these women completed enrollment by returning the base-line questionnaire; 1410 women were randomized into intervention (self-help) and control groups. After deleting 14 ineligible cases, the final sample for analysis contained 1396 subjects. All subjects who completed the five follow-up telephone interviews were paid US\$ 80. In addition, subjects who reported smoking abstinence at any of the telephone follow-ups



were paid US\$ 20 per visit, at which a variety of noninvasive health measurements were made, including height, weight, blood pressure, pulse rate and respiratory peak flow. A saliva sample was taken to validate self-reports of abstinence; at 12 months, the validation rate was 81%.

The intervention consisted of six booklets, mailed sequentially on a weekly basis from the health maintenance organization, and in no way were they identified as connected with UCLA. Thus, we tried to dissociate the Preventive Health Behaviour Study from the non-volunteer smoking intervention. The booklets were targeted initially to a precontemplator population, in the hope of catching the attention of women not presently thinking about stopping smoking. However, the six booklets supplied all the critical information for self-quitting and maintenance. Furthermore, the booklets were glossy, colourful and attractively designed. Issues of particular interest to women, such as weight control, social support, management of negative affect, targeting of women by the tobacco industry, and specific smoking-related health risks, were addressed in special sections.

Unlike the studies described above, the subjects were lighter smokers (mean  $19.2 \pm 12.5$  cigarettes per day) than the US female population, but they reported a similar addiction to cigarettes as the nurses; mean =  $4.4 \pm 0.95$ . On a five-point scale, the motivation to quit was  $3.7 \pm 1.3$  and confidence in quitting permanently was  $2.35 \pm 1.5$ . Both of these indicators are much lower than those in the 'unaided study'. Thus, we have a population of women who are lighter smokers with lower motivation and self-efficacy, who believe themselves to be as 'addicted'. In addition, almost half (47.4%) were in the precontemplation stage of change at base-line, 30.8% were contemplators, and only 21.8% were 'contemplators ready-for-action'. This distribution contrasts sharply with the 'unaided sample' described above.

The results of the study show no difference between intervention and control groups in terms of smoking cessation rates. At one year, 15.3% of intervention and 15.2% of control subjects were not smoking (point prevalence); 3.5% of intervention and 2.4% of control subjects were continuously abstinent. These 12-month point-prevalence rates of quitting are quite similar to those in our other studies, but the continuous abstinence rates are much lower, possibly indicating greater instability in cessation status. Also, a smaller proportion of subjects than in the 'unaided study', but similar to the nurses, had quit for 48 h or longer by the one-year follow-up: 55.5% of intervention and 53.4% of controls. Finally, with regard to the point-prevalence measures of stages of change, by 12-month follow-up, precontemplators had decreased to 21.8%, contemplators had increased to 48.1%, 14.9% were ready-for-action, 8.5% were in action, and 6.8% were in maintenance. There was no difference between conditions, but we shall be doing pattern analyses within groups to see whether the intervention differentially affected the likelihood of stage change. Some studies have found that people in the contemplation stages are more likely to respond to self-help materials by making an effort to quit than people in earlier stages (9,17). In terms of finding a population change in smoking prevalence in the intervention compared to control group, this study was not successful. We shall be probing the data for more sensitive indicators of change and for explanations of the failure to find change, such as the use of materials.

## SMOKING CESSATION IN HEAD-AND-NECK CANCER PATIENTS

We are currently conducting a randomized physician and dentist-delivered smoking cessation programme for patients with newly diagnosed squamous-cell carcinomas of the head and neck. This is the first intervention designed for patients with smoking-related oral cancers and the first to involve surgeons



and maxillo-facial prosthodontists. Persons who stop smoking following a diagnosis of cancers of the upper aerodigestive tract are less likely to develop second primary cancers or recurrences, and they have better overall survival (19-22).

The intervention programme consists of tailored advice to quit smoking, which is delivered following surgery or at the beginning of radiation treatment, and is followed by six-monthly advice booster sessions accompanying regular medical visits. Three special self-help booklets were written for this population: cessation, long-term abstinence and social support by a spouse, family member or caretaker. The booklets were targeted to a cancer patient population who are newly diagnosed and facing difficult treatments, cancer-related adjustments and problems with living (speech, communication, eating, disfigurement, depression and depletion in energy). The special risk of smoking for head-and-neck cancer was illustrated diagrammatically, and both physical and emotional aspects of cancer were discussed for patient and family members. Other features of the programme include quit contracts and reminder postcards for the patients, plus repeated provider training and feedback for the medical personnel. Adherence of patients is being assessed *via* a six-factor comprehensive model (23). In addition to smoking cessation, biomedical outcomes will also be assessed.

Base-line descriptive data for the first 109 subjects accrued show these persons to be older (mean= $57.3 \pm 9.5$  years), more likely to be male (71.6%) and heavier smokers (mean= $23.4 \pm 11.9$  cigarettes per day at current rate and  $33.0 \pm 15.3$  cigarettes per day at maximal rate). We are accruing both current smokers (88.1%) and persons who quit within the past year (11.9%); the latter are at risk for relapse. The means for self-reported addiction are  $4.3 \pm 1.2$ , desire to quit —  $4.2 \pm 1.3$ , confidence in staying quit —  $4.0 \pm 1.3$  for current smokers and  $4.8 \pm 0.6$  for former smokers. To

date, 27.5% of these 109 patients have been treated with radiation only, and 72.5% have been treated with surgery alone or surgery plus radiation. Among the 79 surgical patients, 30.3% have undergone a total or partial laryngectomy, and 69.6% a non-laryngectomy procedure. It will be fascinating to observe the effect of the combined intervention in this high risk population.

## MINORITY POPULATIONS

We have recently received two grants from the National Cancer Institute to design, implement and evaluate smoking cessation interventions in a controlled design for adult black and Hispanic populations in greater Los Angeles, both groups falling within the middle to poorest socioeconomic strata. One population will be reached through the public school system of Inglewood, and the other through the federally funded 'Head Start Programme' for indigent preschool children and their families. In these populations, we shall be using a menu of cessation options, designed to target persons at all stages of readiness to quit smoking. These will include print materials that are drawn from English and Spanish self-help guides — containing simple language, heavily illustrated, and multi-ethnic in orientation. In addition, we shall utilize telephone hotlines, supportive telephone calls, and groups led by indigenous facilitators. A community empowerment model will encourage leadership and participation by persons in the community to reinforce the concept that nonsmoking is an appropriate cultural norm (24). Thus, the principles cited by the consensus report will be incorporated into the research.

In conclusion, at UCLA we have accumulated a great deal of experience with self-help methods and appreciate their potential to reach large populations of persons with minimal expense and maximal flexibility. However, a range of questions remains to be addressed which critically affects the impact of such programmes on their target populations. The



issues of greatest importance, as exemplified by the studies described in this paper, include: (i) the use of volunteer *versus* non-volunteer populations; (ii) readiness to quit smoking and targeting to stage of change; (iii) the use of adjunctive methods combined with self-help materials; (iv) disease severity and its effect

upon outcome; (v) adherence, or the use of programme materials; and (vi) finally, determination of the predictors of successful cessation. This is an exciting era, and we are well equipped as scientists to design studies and data analyses to address these questions.

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# How doctors in developing countries can control tobacco consumption

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A major outbreak of tobacco-related disease and death is approaching in developing countries. With concern and commitment, doctors in these countries can play an effective role in containing this malady in many different ways. Following the second report of the Royal College of Physicians 'Smoking and Health Now', a group called 'Action on Smoking and Health (ASH)' was formed in 1971, whose members are also active in some developing countries such as Sudan, India and Kenya.

## INTRODUCTION

The world's developing countries are on the threshold of a major outbreak of disease and deaths due to tobacco. Other epidemics, such as smallpox, tuberculosis and poliomyelitis, have either been eradicated or are being brought under control due to the persistent efforts of medical scientists, public health workers, and governments. By contrast, tobacco consumption is being promoted actively worldwide by unscrupulous multinational companies who are the agents of a man-made disease without parallel in human history.

Decreasing tobacco sales in developed countries, such as the USA and the United Kingdom have led tobacco companies to look for their profits in Third World countries, and at least three major factors encourage them to do so. These are — the widespread ignorance of the lethal consequences of tobacco, the attraction which tobacco provides to governments for the collection of tax revenues, and the prolonged latency between the initiation of the habit and the diseases it causes. In this way, not only smokers but also governments and whole industries become addicted to tobacco.

Those who set out to control tobacco consumption in developing countries are thus faced with a ruthless industry, tobacco dependent governments, and many addicted and influential smokers. Doctors have usually acted as the advance guard in this battle. They are well aware of the scientific evidence, they see their patients needlessly dying, and they know how ineffective their treatments often are. They find themselves palliating patients who are terminally ill with preventable diseases, and this action makes them frustrated and angry. Doctors, however, usually have a privileged position in society and their opinions carry weight, not only with the public, but also with politicians. Cabinet ministers, like other mortals, fall sick and may more readily respond to health messages in the privacy of the consulting room when examined without their shirts! Members of Parliament, who fail to be impressed by the health statistics on smoking, may be moved to take action when they see patients in hospitals suffering from cancers of the lung or mouth, heart attacks, or leg amputations — especially if they are their own constituents. But sadly, doctors as a whole have not given high enough priority to the prevention of disease. The fascination and excitement of removing a cancerous lung or



replacing blocked coronary arteries exceed that of giving advice on smoking, overeating or physical sloth. Doctors too easily forget that health depends more on pure food, clean air and safe water than on drugs and operations.

As a doctor who practised at the height of the holocaust of smoking-caused diseases in the United Kingdom, I saw many patients with inoperable lung cancer and others crippled with chronic chest disease or dying from coronary heart disease. As a result, some of us joined forces in 1971 to form Action on Smoking and Health (ASH), following the second report of the Royal College of Physicians, which gave us their full support. Since then, we have seen rates of cigarette smoking in the United Kingdom fall from 52% to 31% in men and from 41% to 29% in women. As a result, death rates from lung cancer, chronic bronchitis and heart attacks are beginning to fall, especially in people under the age of 50 years.

This experience, which has been repeated in the USA, Australia and New Zealand, among other countries, has led a number of non-governmental organizations, such as the International Union Against Cancer, to take action to try to prevent similar epidemics in developing countries. Small groups of experienced health workers from both Third World and industrialized nations have been sent to help initiate smoking control activities in over 30 centres, so far.

I should like to describe the experiences we have had in three different countries. As it happens, one nation was a Muslim country, the second was a state with a dominantly Buddhist community in India and the third was a mainly Christian country, although each faced similar problems. I am well aware that in India several active groups are attempting to control tobacco consumption. In each country, it has been a few committed individuals who have made significant progress in the face of considerable opposition.

## SMOKING CONTROL ACTIVITIES

**Sudan:** Postgraduate doctors often become aware of the consequences of cigarette smoking when they get trained in the United Kingdom or other western countries. This experience motivated Dr Mahmoud Alarabi, a consultant physician in Sudan to undertake a prevalence survey of smoking habits in Khartoum soon after his return. The results showed that a majority of doctors and university teachers, as well as a considerable number of students, smoked cigarettes. Sudan is a male-oriented society and until recently few women smoked; but women are now starting to do so, especially those working outside the home, since to some it has become a symbol of independence and equality with men. Doctors became concerned at the growing hazard of tobacco and pressed the Minister of Health to take action. The Association of Physicians, headed by Dr Gizouli Dafalla, who later became Prime Minister, presented the medical facts and brought pressure to bear on members of Parliament and on other leading figures. As a result, a 'Regulation of Smoking Act' was passed in 1983 by the Peoples' Assembly, which banned all cigarette advertising, restricted sales to cigarettes with a tar content of 15 mg or more, placed health warnings on all cigarette packs, and attempted to control cigarette smoking in public places.

In 1984, the Ministry of Health, supported by the International Union Against Cancer and WHO, organized a conference in Khartoum to consider the problem of smoking and health; about 50 delegates attended from East African and Middle Eastern countries. Soon after the conference, Sudan suffered a disastrous famine, together with a civil war in the south. Despite these setbacks, in January 1985 the Sudan Anti-Smoking Society (SASS) was inaugurated and was supported by doctors, politicians, artists, teachers, economists, businessmen and the mass media, together with help from religious leaders. These activities



were undertaken despite the active opposition of British-American Tobacco, the main company importing cigarettes into the country. In 1988, a conference on chest diseases was opened by Prime Minister El Saddig el Mahdi, who gave the campaign his strongest support. He also wrote to all members of the State Council and the Legislative Assembly, informing them of the facts about smoking and urging them to take necessary action. The achievements, so far, in Sudan have been initiated by a small group of concerned doctors; their considerable success should be an encouragement to others in developing countries.

**Ladakh (India):** Ladakh is a remote area in northwestern India, lying between the Himalayas and the Karakoram mountains at an altitude of 3000-4000 m. Following a visit I made in 1985, Dr Tsering Norboo, consultant physician in Leh, decided to take action on the tobacco problem which was developing. Due to the opening of the road to tourists and the military, cigarette consumption had been increasing. Surveys showed that about one-quarter of the men were smokers, but the percentage was even higher in the younger age group. None of the women smoked, but over one-third complained of passive smoking, mainly from their husbands' cigarettes. This condition was often aggravated by the smoke from their kitchen fires, especially in winter.

Following the 1988 'World No Smoking Day', Dr Norboo wrote: "Every section of society was involved in the anti-smoking campaign. All-India Radio broadcast antismoking slogans in Hindi and Ladakhi regularly before the news, which is the most popular listening period. Radio talks and discussions were arranged. All the schools in Leh and the surrounding villages started the prayer period with a 15-20 min talk on the topic. Young boys are approaching me for literature on the subject. Ladakh Action on Smoking and Health (LASH), the Lion's Club, and the Health Department organized a very successful

meeting with the help of the Development Commissioner. All the headmasters, principals, presidents of various clubs, village heads, and a variety of other leaders were present. The radio gave complete coverage, and I now expect wider acceptability of smoke-free homes and work places".

Smoking control is particularly important in Ladakh since so many people there have chest diseases due to chronic exposure to smoky kitchens in winter, to dust storms in spring which can lead to silicosis, and to the prevalence of tuberculosis. Environmental conditions in Ladakh are similar to those in Nepal, where heavy smoking and domestic smoke pollution cause a high prevalence of severe chronic bronchitis. Doctors are anxious to prevent this from happening in Ladakh and give strong support to LASH.

**Kenya:** In contrast to Sudan and Ladakh, Kenya is a dominantly Christian country, and it has a powerful tobacco company. British-American Tobacco (Kenya) has a virtual monopoly on the promotion and production of cigarettes. Mr Gecaga, the Chairman and a son-in-law of Jomo Kenyatta, has strong political influence. Cigarette consumption is rising — until recently at a rate of 8% a year. Advertising is widespread, and an Embassy advertisement welcomes you at the entrance of nearly every town and village.

The London-based British-American Tobacco Co. made £ 36 million profit from its 11 African subsidiaries in 1987, of which £ 2.4 million came from Kenya. In that year, the Kenyan company produced 7481 tonnes of tobacco, of which only 6% was exported, thus yielding about £ 660 000, resulting in a considerable loss to the country's economy.

Doctors at the Jomo Kenyatta Teaching Hospital in Nairobi are very concerned at the growing number of admissions for lung cancer, which has increased from about six to over 40 patients a year in the last 20 years. There is a growing number of deaths from coronary heart



disease, especially among the Asians but also among Africans. A campaign against this smoking hazard has been started by Dr Gershon Amayo and Dr Paul Wangai of the Kenya National Committee for the Prevention of Alcohol and Drug Dependency. A pressure group, Kenya Action on Smoking and Health (KASH), has been started to include all sections of the community.

In 1986, an East African Conference was held, sponsored by the International Union Against Cancer and the WHO, which also stimulated smoking control action in the United Republic of Tanzania and Uganda. Urgent action is needed in East Africa if the present disastrous epidemics of malnutrition and infectious diseases are not to be replaced in the early years of the next century by cancers and vascular diseases caused by tobacco.

## CONCLUSIONS

An effective smoking control policy starts with a few concerned and committed people, usually doctors. The next step should be to produce figures for the prevalence rates of smoking, especially among doctors, medical students, women and children. Such surveys can be carried out by students under the supervision of doctors or epidemiologists, preferably following WHO guidelines.

A survey of smoking-related diseases in the country is important. Since reliable national statistics may not be available, it may only be possible to use hospital discharge records as well as the experience of older doctors who have noted changes in the prevalence of mouth or lung cancer and coronary heart disease in their patients.

An estimate of the future prevalence of smoking-related diseases should be made. Although malnutrition and infectious diseases can cause high mortality rates in children, it is often not recognized that those who survive into their teens and become cigarette smokers carry a one-in-four risk of premature death as

a result. Since over 50% of men, including doctors, smoke in many developing countries, this habit will lead to the loss of many valuable members of society.

The experience of industrialized countries should be studied — such as can be found in the reports of the Royal College of Physicians, the US Surgeon-General and WHO.

An assessment of the untoward effects of the multinational tobacco companies should be made, especially in tobacco-growing countries. In most developing nations, the majority of tobacco grown is purely for internal consumption, and it is an economic drain on the country, quite apart from increasing costs to the health service caused by the resulting diseases. In the minority of developing countries where tobacco is an important cash crop tobacco companies may exert considerable political influence. Opportunities for crop diversification should be pursued (see papers by Sanghvi; Chari and Rao, this volume).

Wherever possible, a scientific report should receive the backing of a prestigious medical body, such as the nation's medical association or college of physicians. It could then be presented to the Minister of Health and to other national leaders and Members of Parliament with the request that legislation be introduced to control tobacco consumption.

This legislation should contain measures to ban all tobacco advertising and sponsorship, to ensure that cigarettes containing more than 15 mg of tar not be sold, to make illegal the sale of cigarettes to children, and to control smoking in indoor public places. Strong, rotating health warnings without attribution to the government or health departments should be introduced, such as 'Smokers die younger' or 'Smoking causes lung cancer and heart disease'.

The price of cigarettes should be progressively raised, since this action is one of the most effective ways of reducing consumption



and usually increases revenues from taxation at the same time. To support these efforts, a request could be made to certain international bodies for advice and help. These include the International Union Against Cancer, the International Union Against Tuberculosis and Lung Disease, the International Organization of Consumer Unions, and the WHO, all of

which are active in this field. This process could lead to a Workshop on Smoking and Health for a group of national leaders, preferably sponsored by the Department of Health and one of the above organizations. Most countries also find the need to set up a small pressure group to ensure that progress in the control of tobacco consumption is maintained.

The first part of the paper is devoted to a discussion of the various methods which have been proposed for the determination of the rate of reaction between a radical and a molecule. The methods are classified into two groups: (a) methods which involve the measurement of the rate of disappearance of the radical, and (b) methods which involve the measurement of the rate of appearance of the product. The first group includes the methods of the half-life, the induction period, and the steady-state concentration. The second group includes the methods of the initial rate, the rate of change of concentration, and the rate of change of optical density.

The second part of the paper is devoted to a discussion of the various factors which influence the rate of reaction between a radical and a molecule. These factors are: (a) the nature of the radical, (b) the nature of the molecule, (c) the temperature, (d) the concentration of the radical, and (e) the concentration of the molecule. The rate of reaction is generally found to increase with increasing temperature and increasing concentration of the radical. The rate of reaction is also found to increase with increasing concentration of the molecule, but only up to a certain point, after which it remains constant.

The third part of the paper is devoted to a discussion of the various theories which have been proposed for the mechanism of the reaction between a radical and a molecule. The most widely accepted theory is the one proposed by Kistiakowski and co-workers, which involves the formation of a transition state between the radical and the molecule. The rate of reaction is then determined by the energy of activation of this transition state. Other theories which have been proposed include the one proposed by Hinshelwood and co-workers, which involves the formation of a complex between the radical and the molecule, and the one proposed by Eyring and co-workers, which involves the formation of a transition state between the radical and the molecule.

The fourth part of the paper is devoted to a discussion of the various applications of the study of the reaction between a radical and a molecule. These applications include: (a) the study of the mechanism of the reaction, (b) the study of the rate of reaction, (c) the study of the effect of various factors on the rate of reaction, and (d) the study of the effect of the reaction on the properties of the system. The study of the reaction between a radical and a molecule is of great importance in many fields of chemistry, including organic chemistry, physical chemistry, and biochemistry.

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## Role of dental professionals in reducing tobacco use

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Although rates of quitting smoking following intervention by dentists are as effective as those after intervention by physicians, dentists, unfortunately, are much less likely to advise and assist patients than are physicians. About 63% of the US population aged five-years and older visit a dental office each year; of these, 75% are under 17 years of age. Recognizing the dentistry's potential impact on tobacco use, the National Cancer Institute began in 1988 to expand participation of dental professionals in its smoking and intervention programmes and to promote their involvement with other organizations committed to creating a tobacco-free society. The Institute is promoting, focusing and coordinating dental initiatives against tobacco use. The year 1990 begins the decade of developing dental commitment, improving service, knowledge and skills and integrating prevention and cessation services into dental practice.

### INTRODUCTION

Dentists and other members of the oral health team can and should be strong allies with other health professions in reducing tobacco use and its terrible consequences. The number and distribution of dentists throughout the world, their education and their one-to-one contact with the public make them effective in this cause.

Dentists could have a major impact on the public's smoking status. This was the principal conclusion of Cohen *et al.* (1) after studying patient rates of quitting after 50 private dental practitioners and their office staff members had used smoking cessation methods previously shown to be effective when used by physicians. In a different study, Cohen *et al.* (2) found that dentists were at least as effective as physicians in persuading patients to stop smoking. They found that asking dental patients about their tobacco habits and strongly urging them to quit typically used only 2-3 min of time, but this effort resulted in

a one-year confirmed rate of quitting of about 8-10%. When the advice was augmented with nicotine replacement therapy, clinic staff time increased to 5-6 min, but success rates also doubled, increasing to 16%. These success rates were consistent with, or better than, results from similar studies of physician practices (3-10).

Unfortunately, the potential impact that dentistry could make on smoking behaviour has been largely unrealized. Gerber *et al.* (11) found that only 17% of dentists, compared to 57% of internists, frequently discussed quitting with their patients who smoked. They found that dentists almost entirely (98%) agree that smoking is extremely dangerous to health, but most (75%) found counselling patients to be a frustrating task. Lack of proper training for the service was evident.

Secker-Walker *et al.* (12) found that many dentists (84%) routinely take a smoking history. Of these, 60% offered advice to stop smoking, but 40% were silent. Just as Cohen



*et al.* (1,2) had observed, about 2-3 min per patient was devoted to this activity. The advice offered most frequently (38%) was for patients to 'cut down', a notably ineffective method. The finding of Secker-Walker *et al.* (12) also suggested a strong need for training.

In the USA, a large proportion of the national population visits dental offices. Hayward *et al.* (13), in a telephone survey of 9352 individuals, found that 63% of persons aged 18-64 years had made at least one dental visit within the past year. This ratio approximates findings from other national surveys (14,15). Hayward *et al.* (13) found that 75% of individuals aged 5-17 years had visited a dental office within the previous year. Major minority populations, i.e., blacks and Hispanics, have disproportionately high smoking rates and experience high rates of smoking-related diseases and death. Hayward *et al.* (13) found that more than half of these special populations visited a dentist in one year.

In 1990, about 163 800 dentists were licensed to practise in the USA (16). If most, three-fourths for example, would routinely include tobacco-use intervention among their services and were 10% effective, they would be responsible for there being 3 million more ex-users each year. In addition, it is significant to note that most children and youth aged 5-17 years visit a dental office each year; these are the years when tobacco is tried and patterns of use are established. If one-fourth of the people who would otherwise start using tobacco could be persuaded by the oral health team against doing so, an additional 250 000 individuals per year would remain tobacco-free.

The National Cancer Institute (NCI), considering such information, concluded that dentists and their staff: (i) are capable of providing effective smoking intervention services, (ii) have regular access to a significant proportion of population, and (iii) would like to be involved, but are in need of intervention training and a coherent strategy for involvement.

Thus, in 1988, the NCI began a major effort to help the oral health team and dental organizations to reach their full potential in this vital health service.

## NCI SUPPORT OF DENTISTRY'S ROLE

In 1989, eight specific activities were begun by the NCI to help define and strengthen the role of dentists in tobacco control. First, a goal was established to highlight the profession's responsibility and opportunity. The statement of this goal is "to ensure that the oral health team and dental organizations are directly, appropriately, and routinely involved in influencing patients and the public to avoid and discontinue the use of tobacco."

The dental goal includes three important concepts. First, it addresses 'tobacco', rather than its subset, 'smoking'. For many years, the dental profession identified itself more with the smokeless tobacco issue than with smoking, even though smoking is also associated with many oral conditions. Thus, the broader 'tobacco' goal may be seen in dentistry as an extension of an existing concern, rather than one that is entirely new. The concept also includes recognition of a responsibility to help smokers who switch to smokeless tobacco and *vice versa*.

The second concept embodied in the goal is the reference to the 'oral health team', rather than to the 'dentist' only. This phrase is a response to the finding that clinical intervention services are more effective when the entire clinic staff is involved than when the physician or dentist acts alone. People in general may find the phrase unfamiliar, but dental hygienists and dental assistants will appreciate that it recognizes their importance in providing services for tobacco use prevention and cessation.

Third, the goal refers to 'dental organizations' and 'the public', as well as to 'the oral health team' and 'the patient'. This concept recognizes professional opportunities to influence the public through dental organizations, community activities and personal example.



Once the goal was defined, the NCI organized a coalition of 10 major national dental associations to act as a focus and coordinating point for dentistry. The group is known as the National Dental Tobacco-free Steering Committee. Nearly all dentists, dental hygienists and dental assistants in clinical practice, education, public service or research are members of one or more of the 10 organizations represented in the committee. The purpose of the committee is threefold: (i) to assess recent developments in strategies for the prevention and cessation of tobacco use, (ii) to define opportunities for involvement of dentists in tobacco control activities, and (iii) to promote cooperation and collaboration between dental, other health professional and public interest organizations at the community, state, national and global levels.

Although dental association representatives help guide the NCI so that its intervention initiatives are compatible with dentistry, feedback to each organization is expected to provide fresh ideas for independent dental action against tobacco use.

An initial activity, for example, is to create a set of comprehensive statements that may prompt dental associations to adopt strong antitobacco policies and position statements and to promote member and association action. Model policies under consideration are being classified into five areas: those pertaining to services, education, research, administration and advocacy.

A third NCI activity is to invite government and private volunteer organizations that have an interest in tobacco use intervention services, in dentistry, or in both, to monitor committee activities and recommendations. Such monitoring agencies include the American Cancer Society, the Office of Smoking and Health, the National Institute of Dental Research, the Centers for Disease Control, the Veterans Administration, the Military Dental Services and the World Health

Organization's Central and Regional Dental Units. These established, recognized agencies and institutions may convert committee proposals into tobacco use intervention programmes in their own dental components, within the context of their particular missions. Conversely, the agencies may offer ideas to various dental associations and collaborate with them.

Fourth, the NCI is developing continuing education programmes for clinicians. Curricula, trainers' guides and office manuals for clinicians were written in 1989. The first dental course was scheduled for 20 January 1990. This training programme is similar to the one developed for physicians, with a few differences that make it consistent with the concepts expressed in the dental goal statement. The NCI is also encouraging dental and dental hygiene schools to train undergraduates and graduates to use scientifically sound tobacco use intervention methods.

Fifth, requests have been made to modify proposed national health objectives for the year 2000 (17), so that objectives on tobacco, cancer and oral health all contain similar and mutually supportive professional education and awareness language. Such a change should ensure that intervention service objectives do not preclude dental involvement. Originally, some draft objectives addressed physicians only. It appears that the final wording will give mandates and direction to intervention roles for dentists, and other health care workers who are professionally in direct contact with the public. It is proposed that the oral health objectives be expressed in two statements that read approximately as follows: (i) by the year 2000, 75% of dentists and dental staff assisting them should routinely ask their patients about their tobacco use, (ii) 35% of dentists should have received specific, applied training in methods for helping people to stop tobacco use.



These objectives for the year 2000 for professional education, awareness and practice are ambitious, but achievable.

Sixth, the NCI is drafting a brief, illustrated guide to tobacco-induced oral diseases and conditions for use in dental clinics for reference. Lesions found in the mouth can be used to help persuade patients to quit. Showing patients their own lesions is more likely to get attention than discussing unimaginable diseases, incomprehensible risk factors or an unfathomable future. In a recent study, Schroeder *et al.* (18) found that only 10% of patients who use smokeless tobacco reported that their dentists had told them that they had lesions in the mouth that could be associated with its use, but independent examinations found that more than 62% had clearly visible degree II and III lesions. The guide will promote careful examinations by including a brief, illustrated description of a common standard examination method.

Seventh, the NCI periodically reports many of the activities described during a variety of dental association meetings and in newsletters and journals. This effort is intended to make practitioners aware of new dental-oriented tobacco use intervention information, the availability of training programmes and support literature, and whom to contact for answers to specific questions. Other communication network ideas are under consideration that might help bring the dental profession 'into the loop' on tobacco issues.

The eighth and last NCI current dental initiative pertains to research applications. Both the NCI and the National Institute of Dental Research fund studies of smokeless tobacco intervention services. These Institutes are jointly planning when and how, with the help of dental and other organizations, such research findings may be best translated into a more effective public service programme against smokeless tobacco products. In

addition, an increasing number of smoked and smokeless tobacco-related issues are finding their way into various dental research agendas.

## EVALUATION PLAN

Dental involvement in tobacco control issues in a focused, multifaceted, coordinated fashion is a relatively new development. Involvement is now centering on plans for the 1990s that support the proposed national health objectives for the year 2000. Information collected in 1989 about tobacco intervention services in dental practice will provide base-line data for evaluating the initiatives described. Data available at the conclusion of the NCI Community Intervention Trial for Smoking Cessation (COMMIT) will be usable during a 1994 mid-course evaluation of the decade's activities. The America Stop Smoking Intervention Study for cancer prevention (ASSIST) is scheduled to be in the field from 1994 to 1998 (see paper by Glynn *et al.*, this volume). Data collection in 1998 and analysis in 1999 should provide excellent information about how dental practice and dental education changed during the 1990s. Findings and conclusions should also form the basis for further action as the new century begins.

## CONCLUSION

Although the activities described in this paper began primarily in the USA, they could and should become global. Indeed, national boundaries do not limit current activities. WHO, at least one of its regional offices, and the chief dental officers employed or retained by various country ministries of health are periodically advised about new dental roles and NCI initiatives. Exchanges of information and cooperation between countries are encouraged.

Patients in industrialized countries are generally health conscious and understand the role of personal responsibility for health outcomes. Dental teams can relate to most people in such countries through individual practice



relationships. There are few dental practices in less developed countries, so the capacity to reach most people directly is lacking. Relatively few people may receive dental care. Those fortunate few, however, are often the very people who hold the destiny of a country in their hands. Therefore, dental involvement

in countries with extreme limitations in resources can still pay enormous dividends. We can reach no other conclusion than that the dental profession is an important link in the chain of activities needed to significantly change tobacco use knowledge, beliefs, and practices of people throughout the world.

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# The public health practice of tobacco control

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Twenty-five years after the publication of the first US Surgeon-General's Report on the Health Consequences of Smoking, considerable progress against tobacco use has been observed in the USA. The public health practice of tobacco control has been refined during this period, and several essential elements in this practice may be identified: (i) surveillance systems, including behaviour process and disease outcomes to control tobacco have been established; (ii) disease impact estimates, i.e., smoking-attributable mortality, morbidity and economic costs, have provided potent information to policy makers and public health officials; (iii) policies that restrict smoking in public places and the excess of minors to tobacco have assisted in changing the social milieu supporting tobacco use in the USA; (iv) community planning and coalition-building have become mainstays in the complex task of tobacco controls; and (v) public information campaigns using several different media have been extremely effective in changing the public's perception of tobacco. Despite the significant progress against tobacco, and downward trends in its use, 50 million Americans continue to smoke.

## INTRODUCTION

As a public health problem, tobacco use may not be unlike communicable disease, with which practitioners of public health have great familiarity. The public health practice of communicable disease control incorporates strategies for surveillance, case finding, clinical treatment, containment, immunization, public policy development and goal-setting. Many of these strategies can be applied to the control of chronic diseases, especially those caused by tobacco. Tobacco use is itself a disease of addiction, and it is responsible for 2.5 million deaths worldwide (1).

The 1964 Report of the Advisory Committee to the US Surgeon-General provided the scientific information needed to launch an effective, sustained public health campaign against tobacco (2). This campaign was described most recently in the Surgeon-General's 1989 Report, *Reducing the Health Consequences of Smoking — 25 Years of Progress* (3).

Despite the notable successes of the last 25 years, tobacco use is still widespread in the USA.

Recently, tobacco prevention and control activities have focused on the individual states. It is within the states' jurisdiction to protect the public against environmental and infectious hazards.

This paper summarizes the progress made against tobacco use, outlines the essential elements of the public health practice of tobacco control, and describes the future directions of public health activities against tobacco use in the USA.

## TWENTY-FIVE YEARS OF PROGRESS

The 1989 Surgeon-General's Report documents that knowledge of the health consequences of tobacco use has expanded dramatically since 1964; programmes and policies for controlling the hazards of tobacco use have



also proliferated. The conclusions of the report highlight important gains in preventing tobacco use and tobacco-related disease and emphasize areas of continuing concern. The conclusions are: (i) The prevalence of smoking among adults decreased from 40% in 1965 to 29% in 1987. Nearly half of all living adults who ever smoked have quit. (ii) Between 1964 and 1985, approximately three-quarters of a million smoking-related deaths were avoided or postponed as a result of decisions to quit smoking or not to start. Each of these avoided or postponed deaths represented an average gain in life expectancy of two decades. (iii) The prevalence of smoking remains higher among blacks, blue-collar workers and poorly educated people than in the overall population. The decline in smoking has been substantially slower among women than among men. (iv) Smoking begins primarily during childhood and adolescence. The age of initiation has fallen over time, particularly among females. Smoking among high school seniors levelled off from 1980 through 1987 after previous years of decline. (v) Smoking is responsible for more than one in every six deaths in the USA. Smoking remains the single most important preventable cause of death in our society (3).

The *per-caput* consumption of cigarettes in the USA is a sensitive measure of the remark-

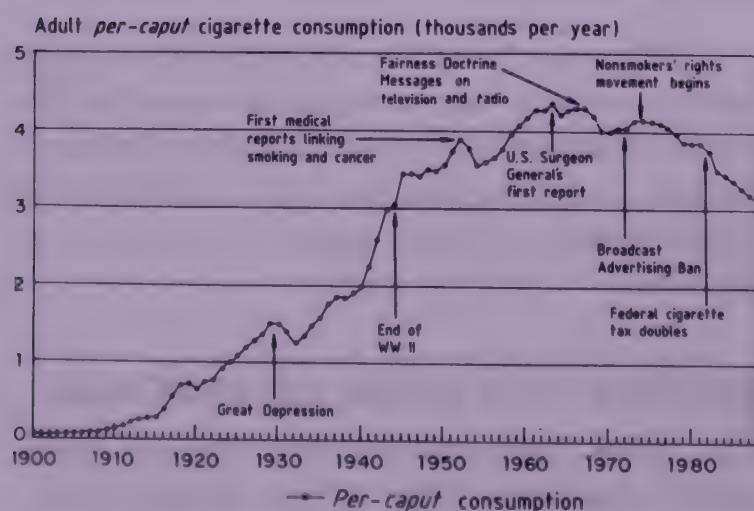


Fig. 1. Adult *per-caput* cigarette consumption and major smoking and health events, USA, 1900-85 (source: USDA, 1989)

able change in smoking behaviour over the last few decades (Fig. 1). Significant events in the campaign against smoking included the first scientific reports on tobacco and its association with cancer, the release in 1964 of the Surgeon-General's Advisory Committee Report (2), the elimination of tobacco advertising from television (after the 'Fairness Doctrine' had mandated such effective anti-smoking television spots that the tobacco companies voluntarily agreed to accept the television advertising ban), the nonsmokers' rights movement (accompanied by the proliferation of clean indoor air policies), and the doubling of the Federal excise tax on cigarettes. Economic disasters such as the Great Depression of 1929-31 and World War II suppressed cigarette consumption because of decreased disposable consumer income. The current decline in *per-caput* consumption cannot be attributed to one event or even a series of identifiable events. Instead, it reflects a changing social milieu in which smoking is no longer seen as fashionable, healthful and safe. With this psychosocial change in attitudes towards tobacco use, the public health practice of tobacco control has evolved.

## ESSENTIAL ELEMENTS OF TOBACCO PREVENTION AND CONTROL

**Surveillance:** Surveillance of disease incidence and the prevalence of tobacco use is critical to assessing the severity of the public health problem and to evaluating changes in disease status resulting from control measures. Surveillance systems must be simple, informative, uniform and sensitive to changes in disease status. For tobacco use, the following surveillance items must be reported periodically:

**Adult knowledge, beliefs and behaviour:** This information indicates the coverage of public information and education campaigns and permits identification of subgroups that may need additional attention.

In the USA, national surveillance of adult smoking behaviour is accomplished through



the National Health Interview Surveys (NHIS) and the Adult Use of Tobacco Surveys (AUTS). Data from the NHIS (4) show that smoking prevalence declined for both men and women between 1973 and 1985, with a steeper rate of decline for men (Fig. 2). It is predicted

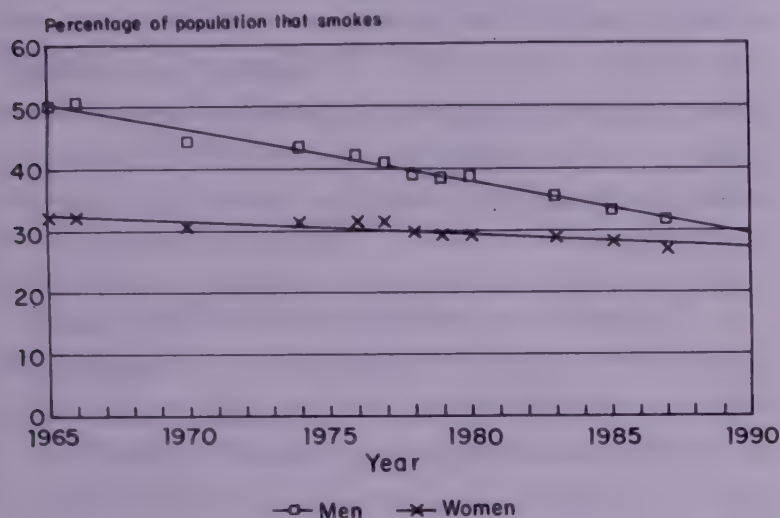


Fig. 2. Prevalence of smoking among adults 20 years old or older, USA, 1965-87 (source: ref. 3)

that by the late 1990s smoking will be more common among women than among men in the USA (5). Low educational status has been found to be the single most important predictor of slow change in current smoking prevalence (6). Thus, national goals should focus on reducing smoking among women (especially young women) and among all persons with low educational attainment.

The AUTS found (3) that knowledge of the health consequences of smoking increased significantly between 1964 and 1986 (Table 1). The data show that progress is being made with public awareness of the health consequences of smoking. Children and adolescents may need additional educational efforts, so that they also recognize the health hazards before experimenting with tobacco.

**Adolescent knowledge, beliefs and behaviour:** In the USA, about 90% of smokers begin to use tobacco before the age of 21 (3). Assessing knowledge, beliefs and behaviour among children and adolescents is a critical component

of a tobacco-use surveillance system. Useful trend data have been provided by the National

Table 1

Percentage of US adults who believed 'smoking causes disease' 1964 and 1986<sup>a</sup>

Year and smoking status	Disease		
	Lung cancer	Heart disease	Lung disease
<b>1964</b>			
Smokers	53	32	42
Nonsmokers	74	41	55
<b>1986</b>			
Smokers	85	71	85
Nonsmokers	95	83	91

<sup>a</sup>Source: Office on Smoking and Health, adult use of tobacco surveys, 1964 and 1986

Institute on Drug Abuse High School Seniors' yearly survey (7). The prevalence of daily cigarette smoking among high-school seniors decreased from 29% in 1975 to 21% in 1980, after which it levelled off at 18-21% (Fig. 3). The prevalence of smoking among females has consistently exceeded that among males since 1977, although a part of this difference may be due to increased use of smokeless tobacco

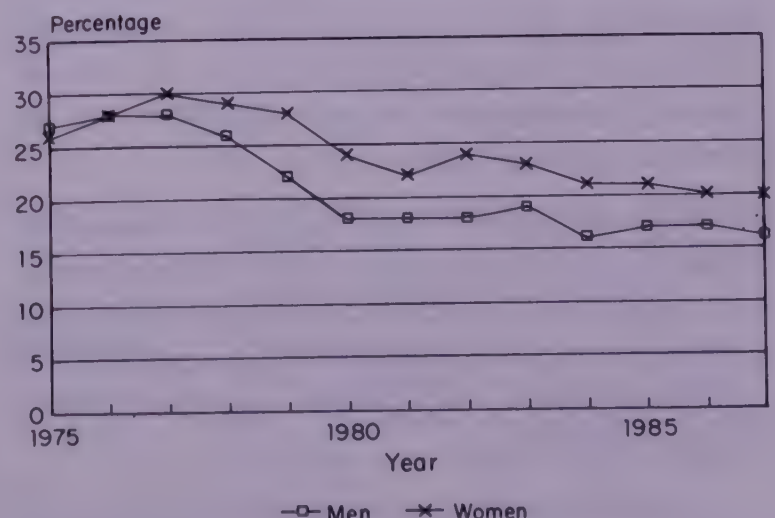


Fig. 3. Percentage of high-school seniors reporting daily cigarette smoking, USA, 1975-87 (source: ref. 7)



among young men over the last two decades (8). The age of initiation for smoking is decreasing (3), which indicates that national programmes should target young persons.

*The tobacco-control procepts (policies, laws, programmes and educational programmes):* In 1989, the Association of State and Territorial Health Officials (ASTHO) surveyed all state health departments about public health control activities within each state. These activities included developing tobacco or chronic disease coalitions, tobacco-control plans, surveillance systems, economic incentives and disincentives, clean indoor air policies, laws restricting minors' access to tobacco products, and others. States can use the results of this survey when comparing their activities with others, measuring the progress of programmes against tobacco and evaluating behavioural outcomes in different populations (9).

When national or state goals call for widespread policies, such as clean indoor air at all worksites, then surveillance systems should be established to follow the spread and coverage of these policies. Data can be obtained from sources such as business groups and unions. If schools are to be tobacco-free, then school boards may also wish to establish systems by which progress towards these goals can be measured. In 1989, the National School Boards Association found that 95% of school districts in the USA had a written policy on smoking in schools and that 17% of schools banned smoking on school premises or at school functions (10).

**Problem assessment:** The second element of tobacco control activities in the USA is problem assessment, which is a detailed analysis of current behaviour, tobacco consumption, current programme capabilities and the disease impact of smoking.

The disease impact measures used in the USA are both epidemiological and economic. The critical calculation in estimating disease impact is the attributable fraction formula:

$$\text{Smoking-attributable fraction} = \frac{p(RR-1)}{p(RR-1)+1}$$

where  $p$  is the prevalence of smoking and  $RR$  is the relative risk of death from a particular disease for smokers compared with 'never-smokers' (11). The relative risk for 14 smoking-associated conditions was reported in the Surgeon-General's 1989 Report (3). Using those values and current smoking prevalence data, it was estimated that 390 000 deaths were attributable to tobacco use each year in the USA (3).

Economic estimates have also been made of the direct costs of medical care and indirect losses due to disability and premature mortality. One estimate is approximately US\$ 65 billion in smoking-attributable economic losses per year (12).

Each state has individualized its estimate of the impact of smoking-attributable disease by using software specifically designed for this purpose (13). Results were reported to each member of the US Congress by the Secretary of Health and Human Services, and results appeared in numerous local newsletters, state medical journals, and state tobacco reports (14). The data are often very useful to policymakers who need to quantify the disease impact of smoking and compare it with other risks (15).

**Policies and programmes:** Interventions against tobacco must be multifaceted; no single intervention will be successful without scientifically-based public education and community-based activities, policies and legislative support. Interventions can be promoted through several channels (Table 2) and measured through several resources. If a particular goal is set — for instance, that all health care providers will advise their patients to quit smoking at every opportunity — then some form of monitoring of this activity must occur. Monitoring could take the form of public surveys or, for physicians, chart reviews.



In the USA, clean indoor air laws have become more widespread and stronger over the last several years (Fig. 4). Thus, a trend has begun that may help convince states to strengthen their laws as part of a larger

**Table 2**

*Examples of intervention activities*

#### Health care system

- Motivate smokers to seek assistance for cessation from health care providers.
- Train physicians, dentists and pharmacists in cessation techniques.
- Expand cessation programmes and funding sources.

#### Worksites

- Promote changes in smoking behaviour at the worksite through presentations, posters and newsletters.
- Support worksite cessation programmes by offering self-help manuals, audiovisual activities and economic incentives.
- Develop smoke-free worksite policies.

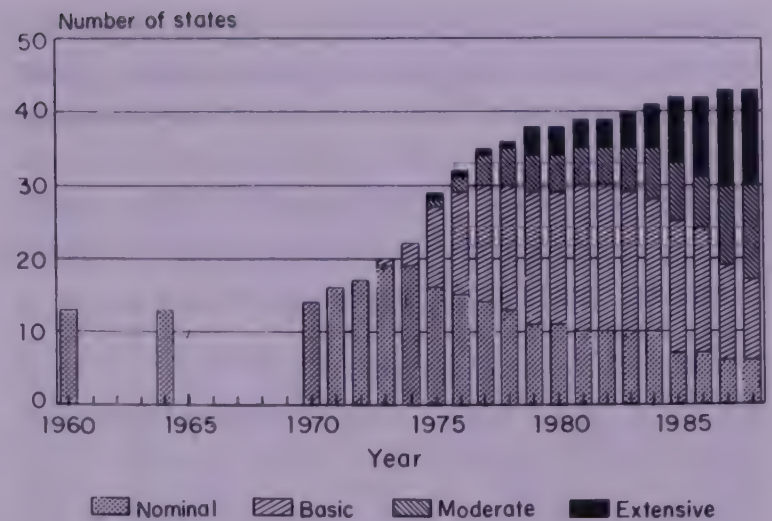
#### Community organizations

- Present information about the health and economic consequences of tobacco use at organization meetings.
- Promote community cessation resources and self-help programmes of large organizations.
- Promote smoke-free meetings and events.

#### Schools

- Mandate tobacco prevention as part of the school curricula.
- Train teachers in prevention and cessation skills.
- Promote parental cessation through actions of children.
- Promote smoke-free policies for school buildings, sports events and other school activities.

national effort. However, the same trend is not true for laws restricting access to tobacco by minors. Very few states have even modestly strong enforcement of restrictions on the purchase of tobacco products by minors (Table 3). In future plans for improving tobacco-control activities, additional attention must be given to strengthening these restrictions and enforcing them.



**Fig. 4.** Number of states with laws regulating smoking in public places, by year and type of law, USA, 1960-88

**Table 3**

*Restriction imposed by laws on minors' access to cigarettes and other tobacco products*

<b>None</b>	No restriction on sale of cigarettes or other tobacco products to minors
<b>Nominal</b>	Law banning sale of cigarettes to minors (minimum age requirement stated). In some places, the law applies to all tobacco products.
<b>Basic</b>	Statewide regulations for sale or distribution of tobacco products to minors (minimum age stated) with penalties of either a fine and/or imprisonment. Bans or restricts access to vending machines by minors
<b>Moderate</b>	Basic regulations that also require visible warning signs at points of sale about the illegality of the sale of tobacco products to minors. Requires a license to sell tobacco products that can be revoked or suspended for selling to minors.
<b>Extensive</b>	Moderate regulations with bans on free distribution of tobacco samples. Mandates enforcement and commits resources for enforcement through earmarked license fees

One effort that may inhibit young people from smoking is increasing the excise tax on



cigarettes (16). Currently, all states impose a tax on each package of cigarettes sold. These taxes range from 2 cents to 40 cents per pack, and they are generally lowest in the tobacco-producing states (17). Recently, portions of excise taxes have been earmarked by some states to fund tobacco-control programmes.

**Public information campaigns:** Figure 1 and Table 1 show that public information campaigns have considerable power. In the USA, media campaigns have been developed for specific groups (minorities, young women and children). Unfortunately, the tobacco industry has also targeted many of these same groups, and analysis of this targeting reveals disturbing and insidious marketing techniques (18).

Communications systems among various public health providers, advocacy groups and non-governmental organizations need to be developed and strengthened (19). These networks permit the rapid dissemination of information and exchange of ideas. Electronic bulletin boards and monthly newsletters have been developed in the USA to help these processes. Training constituency groups (in particular, health department personnel) in media relations is another component of successful public health communications campaigns. These groups can then disseminate to the public scientific information about tobacco-related disease and the need for tobacco-control programmes.

Social marketing is a technique for creating a market for a particular product or service (20). Social marketing can also create a milieu in which tobacco use is no longer the norm, thus facilitating change among users and discouraging young persons from beginning to use tobacco. Public information campaigns are the cornerstone of social marketing efforts.

**Coalition building and community planning:** Coalitions have become an integral part of tobacco-control activities in the USA. The further a coalition extends beyond the health

community, the greater ownership the entire community exerts over tobacco-control initiatives. Coalitions may represent public health officials, health care providers, advocacy groups, voluntary organizations, business groups, religious groups, government officials, the insurance industry, the legal profession, the military, labour organizations, economists, educators, advertisers and communications specialists. Activities of coalitions include developing and implementing tobacco-control plans, public information programmes, and public and professional education programmes. Coalitions also sponsor research and evaluation. Among the 50 states and the District of Columbia, four states have no coalition, 25 states have modestly strong coalitions, 15 states have moderately strong coalitions, and 7 states have strong coalitions (21).

According to the ASTHO survey, nine states have separate public health plans for tobacco use, and 16 states address tobacco use as part of another programme plan (21). To assist states with tobacco-control plans, ASTHO analysed existing plans and published a guide for their development (9,22). The steps for developing a tobacco-control plan include the following: take advantage of national expertise; establish a coalition or advisory group; assess the tobacco problem; develop the mission, goals and objectives of the plan; analyse existing tobacco-control potentials; package and market the plan; and evaluate and revise the plan.

National objectives for the year 1990 included improved health status from the reduction of tobacco use, increased public and professional awareness, improved services and protection, and improved surveillance and evaluation (23). Evaluation methods for tobacco-control activities are still rather rudimentary. Evaluation is difficult because of the unique nature of the tobacco-use epidemic. First, outcomes change very slowly in response to extensive campaign efforts. For example, the



prevalence of adult smoking is decreasing at only 0.6% per year in the USA (4); even after 25 years of change, only recently has the lung cancer mortality rate begun to level off among men (23). A 20-30-year lag period in the expression of chronic disease makes it difficult to measure the success achieved during the last 25 years of changing smoking behaviour in the USA.

Second, the rates of voluntary participation in cessation activities are low (80% of smokers quit on their own) (25), and rates for abstinence achieved through such programmes are low (26). Moreover, medical insurance does not, as a rule, cover payment for such programmes, and cessation programmes are often not appropriately designed for, nor accessible to, the most resistant populations. Thus, the proliferation of smoking cessation services may not be associated with widespread behavioural changes.

Third, behavioural change in response to policies, such as those restricting smoking in public places, is difficult to evaluate. In places where evaluation studies have been carried out (worksites), some policy changes have resulted in no change in overall cigarette consumption, some have been associated with a decrease in the daily consumption of cigarettes, and some have been associated with a decline in the prevalence of smoking (27). Yet, such policies contribute to an overall social norm of not smoking.

Finally, the tobacco industry has mounted a massive rear-guard action against restrictive policies on smoking and against economic interventions against the industry. About US\$ 3.5 billion are spent yearly on tobacco advertising; tobacco is the second most common subject of advertising in the printed media and the most common in the outdoor (billboard) media (28). In addition, each state and nearly every local jurisdiction considering tobacco legislation is pressured by the powerful tobacco lobby. Grassroot efforts, including

referenda, can be expensive and frustrating for groups not funded for and not trained in political processes.

## THE FUTURE OF TOBACCO-USE PREVENTION AND CONTROL

Tobacco-control efforts in the USA will continue to encourage state and local activities. The American Stop Smoking Intervention Study for Cancer Prevention (ASSIST) will begin in 1993 (see paper by Glynn *et al.*, this volume). This multistate programme will coordinate, provide training for, and evaluate efforts to prevent and control tobacco use in 20 areas (entire states or large metropolitan areas) through 1998 (9).

California has achieved heretofore unimaginable funding levels for tobacco control through the passage of Proposition 99, a public initiative that increased the state excise tax on cigarettes, the revenues from which are directed, in part, to tobacco-related education. In the next few years, the question, 'If we had enough money, what could we do to prevent tobacco use?' may be answered in that State. About US\$ 155 million have been earmarked for the health education component of the appropriations bill attached to this successful initiative. A substantial portion of these funds will be directed to a communications campaign that will be thoroughly evaluated (29).

In 1988, the governors of eight western states initiated the Rocky Mountain Tobacco-free Challenge, a regional effort intended to reduce the prevalence of tobacco use and of chronic diseases associated with it. The challenge will continue until the year 2000; key elements include increased community interest, strengthened interstate and intrastate collaboration, promotion of state activities for reducing tobacco use, and long-term evaluation of tobacco-related policies. Other regions of the country may adopt this innovative, competitive approach (30).



International cooperation has begun between the Office on Smoking and Health and the Pan American Health Organization (PAHO). In 1992, a joint report on smoking in the Americas will be produced by the PAHO and the US Surgeon-General. This report will highlight the changing tobacco-use environment in developing countries and emphasize the need to prevent chronic diseases associated with tobacco use. As tobacco use becomes less common in the industrialized world, it is becoming more of a problem in many non-industrialized countries (31).

## CONCLUSIONS

Despite significant progress made against tobacco use, over 50 million Americans continue to smoke. The trend in tobacco use is downward in the USA, and several high risk groups, including young people, minorities, people with low educational attainment and

pregnant women, have been targeted for future interventions. The public health practice of tobacco control continues to evolve, and methods for evaluating tobacco-control activities need further development. Public health efforts for controlling tobacco use differ somewhat from those used to control infectious diseases, but they incorporate several of the same principles. These principles involve scientific information, public policy, mass media, social marketing techniques and community-based programmes to affect change. No single intervention will stop the tobacco epidemic. Public health activities for controlling tobacco use need continual assessment and evaluation; as successful strategies emerge, they should be adapted to different cultural and social environments. Unfortunately, the chronic diseases resulting from the epidemic of tobacco use will be measurable for decades, both in developed and developing nations.

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# **Cancer prevention through a national programme of research into the control of tobacco use: the experience of the US National Cancer Institute**

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Tobacco use has been a part of US culture for over 400 years, predating the arrival of Columbus and the early settlers. Currently, the *per-caput* consumption of tobacco in the USA is 2.8 kg, of which 2.5 kg are consumed in the form of cigarettes. Tobacco use is harmful in many ways. Since the publication of the first Surgeon-General's Report on Smoking and Health in 1964, there have been several notable efforts by different agencies to control tobacco use in the USA. One of the most comprehensive effort is that of the National Cancer Institute. The focus of the programme is on the sequence of research-to-applications, ranging from nearly 50 large intervention research trials begun in 1984 to an 11-site Community Intervention Trial (COMMIT) begun in 1988, to a 17-state American Stop Smoking Intervention Study (ASSIST) for cancer prevention which began in 1991.

## **INTRODUCTION**

At the heart of all strategies to reduce the burden of mortality, morbidity and disability associated with tobacco use is maintaining an understanding of the substantial and expanding body of scientific knowledge about the health consequences of smoking. Thousands of studies detail the numerous and severe health consequences of tobacco use, and a succession of Surgeons-General have reviewed and summarized the health effects associated with smoking and other forms of tobacco use. In order to facilitate understanding of the strategies now being used to reduce tobacco use in the USA, highlights of these data are reviewed below.

## **TOBACCO USE AS A CAUSE OF CANCER**

Knowledge of the relationship between tobacco use and health stems from clinical

observations about cancer, the first disease to be linked to tobacco use. According to one historian, Dr John Hill is credited with the first published report linking tobacco use and cancer, as early as 1761, in his work, 'Cautions Against the Immoderate Use of Snuff' (1).

The first major development in the modern history of the effects of smoking on health occurred in 1950 with the publication of four retrospective studies on smoking habits among lung cancer patients and among controls (2-5). Although many researchers accepted the findings of these early retrospective studies as conclusive proof that smoking was etiologically associated with lung cancer, other investigators turned to prospective investigations in which large numbers of healthy individuals were enrolled in studies and followed over time. Results from these studies documented that smoking not only substantially increases the risk of developing lung cancer, but it



increases the risk of developing cancers at other sites as well as noncancerous diseases (6-8). By the time the Surgeon-General's Advisory Committee on Smoking and Health was established in 1962, eight major prospective studies were already under way or planned. Studies were being conducted in the USA, the United Kingdom and Canada; others were in various stages of development in Japan and Sweden.

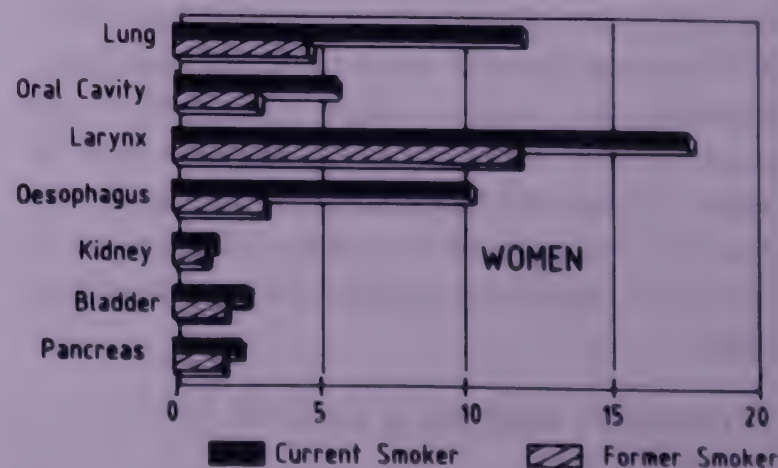
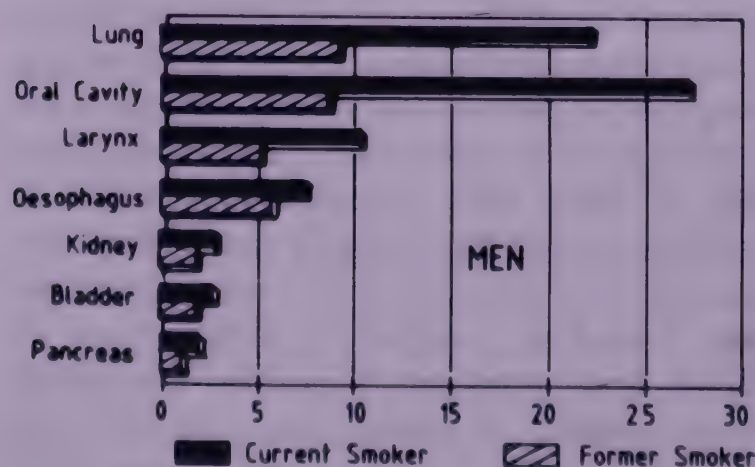
The largest of these, the American Cancer Society (ACS) 25-State Study, was initiated in 1959 and involved more than 1 million persons. These individuals were followed prospectively for 12 years. In 1982, the ACS initiated a new study in which more than 1.2 million men and women in all 50 states will be followed every two years. The ACS 50-State Study provides important, new information concerning the risks of smoking and tobacco use for the individual and the total public health dimension of the disease burden due to tobacco use for the US population (9,10).

Figure 1 shows the risk for male and female smokers of developing cancer at a particular site, as derived from the new ACS prospective study of 1.2 million persons followed for four years. Furthermore, applying national smoking and cancer mortality rates to the new ACS data provides an estimate of the total number of excess cancer deaths attributed to smoking for the US population. For cancers at

the major smoking-related sites, smoking is responsible for approximately 140 000 cancer deaths annually. Because these estimates do not include other sites which are now thought to be associated with cigarette smoking (i.e., stomach, uterine and cervix), or those related to exposure to environmental tobacco smoke by nonsmokers (about 5000 annually), it can reasonably be stated that the total cancer burden due to smoking is probably in excess of 150 000 deaths annually. Overall, nearly one-third of all cancer deaths are considered to be directly related to tobacco use in the USA each year.

### SMOKING AS A CAUSE OF OTHER DISEASES

Smoking and tobacco use are related not only to substantial numbers of cancer deaths but also to deaths from many other diseases and conditions. Figure 2 provides estimates for smoking-related risks for a number of these diseases. Although the risk of death for many of these causes is usually lower than those for lung cancer, they represent a significant number of premature deaths because of their total influence on national mortality patterns. The risk for smoking-related coronary heart disease, for example, is much smaller than the risk for lung cancer; but because coronary heart disease is responsible for more deaths nationally than any other cause the number of smoking-related deaths from this cause is large



Source: ACS 50 State Study      Nonsmoker risk set at 1.0

Fig. 1. Relative risks for cancer mortality among current and former smokers by site and gender



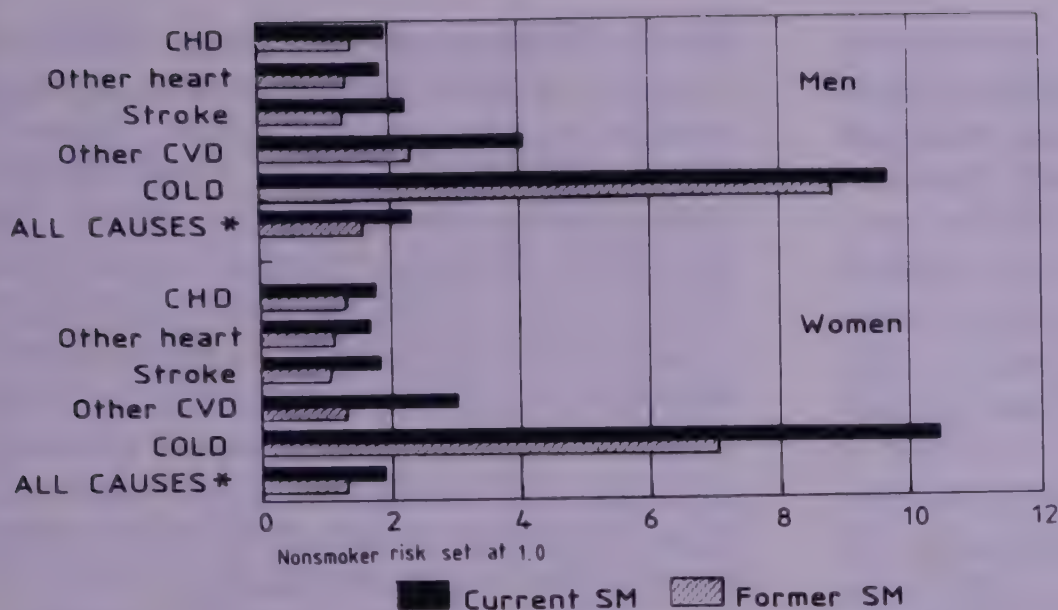


Fig. 2. Relative risks for mortality from other diseases caused by smoking

\* Includes cancer and all other diseases combined  
Source: ACS 50 State Study

(approximately 115 000 deaths in 1985 alone). Overall, smoking is responsible for nearly 400 000 deaths annually in the USA, representing nearly one in every six deaths. Increasingly, proportionately more deaths are due to cancer than the other major causes, and there is no longer any question that tobacco use, particularly in the form of cigarettes, is the primary cause of premature mortality in the USA.

## TRENDS IN CIGARETTE AND TOBACCO USE RATES

Accurate data on trends in tobacco use are needed to estimate the magnitude of the tobacco use problem and its distribution among major socioeconomic groups in the USA, to predict the future course of tobacco-related disease, and to target public health interventions to those people at highest risk of tobacco use and tobacco-related disease.

## HISTORICAL PERSPECTIVE

Tobacco use has been a part of American culture for more than 400 years, predating the arrival of Columbus and the early settlers. The use of cigarettes, however, is of relatively recent origin, having gained widespread acceptance only during this century.

Most of the tobacco consumed before 1900 was in the form of smokeless tobacco, but widespread adoption of cigarette smoking began in 1913 with the introduction of the first blended cigarettes. These cigarettes represented an entirely new generation of smoking products that were easily inhaled compared to their earlier counterparts, thus directly exposing the lungs and other organs to the dozens of toxic and carcinogenic constituents found in tobacco smoke. Simultaneously, use of smokeless tobacco decreased, due in part to concern about the spread of tuberculosis and the advent of anti-spitting laws. By 1921, more tobacco was being consumed *per caput* in cigarettes than in any other single tobacco product, and as early as 1934, it accounted for more than half of all tobacco consumed.

The use of cigarettes accelerated during and immediately following World War I, particularly among men. By the early 1920s, a majority of men were estimated to be regular cigarette smokers, having switched from other forms of tobacco use; however, smoking by women was still not socially acceptable.

In fact, when successive age groups of men and women are examined, it is readily apparent that large numbers of men became regular smokers two to three decades earlier



than women (11). Furthermore, smoking behaviour among older men and women differed substantially. It is only in the more recent age groups (i.e., beginning about 1940) that most women began smoking before their late twenties or early thirties, whereas the vast majority of men initiated regular smoking while in their teens. Peak consumption occurred in 1952 when 5.9 kg of tobacco were consumed per person; of this amount, 4.7 kg were consumed in cigarettes. Today, cigarettes still account for the vast bulk of all tobacco consumed (2.5 of the 2.8 kg tobacco consumed *per caput* in the USA); however, the total weight of tobacco *per caput* and the total weight of cigarette tobacco *per caput* are only half what they were 40 years ago.

The first large-scale survey to determine smoking prevalence was conducted in 1955

by the National Cancer Institute (NCI) in response to early findings linking cigarette smoking to risk for lung cancer. Figure 3 depicts the changing nature of smoking prevalence among men and women between 1955 and 1987. Following decades of increased cigarette use, smoking prevalence and overall cigarette consumption began to fall during the 1960s as a result of the first Report of the Surgeon-General in 1964, publicity surrounding mandated warning labels, and other measures undertaken to inform the public about the hazards of cigarette smoking.

Men responded more quickly than women to these first warnings. Between 1966 and 1978, smoking rates declined by nearly 15% among men, while there was little change among women. Since the mid-1970s, however, smoking has declined in both men and women with each successive survey. This trend has continued into 1987 — the last year for which detailed national data are available.

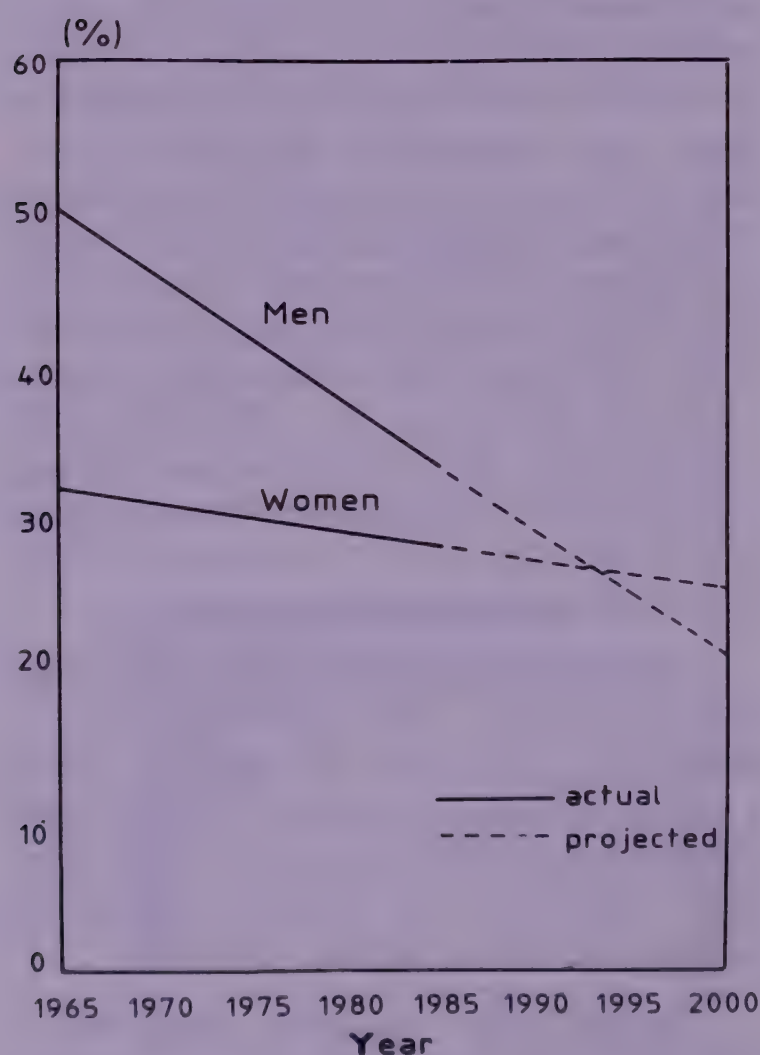


Fig. 3. Trends in US adult smoking prevalence (source: ref. 13)

## CURRENT PREVALENCE OF TOBACCO USE

In 1987, the National Health Interview Survey (NHIS) assessed health practices known to affect cancer morbidity, mortality and survival. Included in this survey were questions regarding current and former use of various tobacco products and the public's perception of smoking and tobacco use practices on health. A detailed analysis of the 1987 NHIS cancer supplement was summarized by Schoenborn and Boyd in 1989 (12). Some key findings that are illustrative of the current use of tobacco in the US are highlighted below.

**Differences by gender:** Smoking among all adults (both men and women 20 years of age and older) was 29% in 1987, the lowest reported figure since the Government began collecting information in 1955. Smoking rates remain higher among men compared to women; however, the gap between the genders is narrowing (Fig. 3), and if present trends



continue, women may surpass men in smoking prevalence by the mid-1990s (13).

**Racial/ethnic smoking prevalence:** Among the largest US racial/ethnic groups, black males have the highest reported current cigarette use rates (39%) and Hispanic females the lowest (18%). White and black females have identical smoking rates (28%), a pattern that has been consistently observed for nearly two decades. Among all major racial and ethnic groups, the highest rates are generally seen in middle-aged groups, after which smoking declines. Whites of both sexes smoke more cigarettes per day than other groups, and they have higher rates of heavy smoking (>25 cigarettes daily).

**Teenage cigarette smoking:** While periodic, systematic surveys to assess smoking among the young have not been conducted, data from other surveys that include significant numbers of teenagers or high-school students do provide insight into current adolescent cigarette use. Data from the National Institute on Drug Abuse (NIDA) High School Seniors Survey shows that smoking by seniors has remained nearly constant at just below 20% since 1980, after several years of decline. The 1985 NIDA Household Survey supports this finding, with 16% of teenagers (12-17 years of age) reporting having used cigarettes in the past month. This figure is lower than in 1977, but it represents virtually no change from 1982. Two smaller studies (14,15) suggest that smoking among school dropouts is considerably greater than among young people still in school, with prevalence rates as high as 75%.

**Other forms of tobacco use:** Several questions concerning other forms of tobacco use were included on the 1987 NHIS. Use of these products is primarily a male phenomenon; fewer than 1% of all women use other forms of tobacco. Slightly more than 6% of males used some form of smokeless tobacco regularly in 1987, about 3% used pipes, and 5% smoked cigars (16).

Use of smokeless tobacco products by young adolescent males appears to be a growing problem. Teenage boys, 16-19 years of age, reported a 300% increase in the use of snuff and a 250% increase in the use of chewing tobacco between 1970 and 1985. A similar pattern of increased use occurred among younger adult males (20-29 years of age) during this same period (16).

## US STRATEGIES FOR THE CONTROL OF TOBACCO USE

Efforts to control tobacco use in the USA accelerated after publication of the first Surgeon-General's Report on Smoking and Health in 1964. These efforts have been multi-pronged, including the development of numerous prevention and cessation programmes, public information campaigns, legislative initiatives, advocacy activities and others. A wide range of organizations in the Federal sector (e.g., Office on Smoking and Health, National Heart, Lung, and Blood Institute, National Institute on Drug Abuse), voluntary agencies (e.g., American Lung Association, American Cancer Society, American Heart Association, March of Dimes), and others (e.g., American Medical Association, State Health Departments, Doctors Ought to Care), have been closely allied in efforts to control of tobacco use.

Because the range of activities and organizations involved in these efforts is wide-ranging, a considerably more detailed document would be necessary to describe them fully. Therefore, as an example the most comprehensive of these efforts, the tobacco use control programme of the NCI will be described in some detail.

## REVIEW OF NCI INITIATIVES TO CONTROL TOBACCO USE

The NCI has a long history of smoking control efforts. After the first studies linking smoking with lung cancer in the early 1950s, the NCI soon included smoking as part of its research



agenda. Since then, it has established a comprehensive cancer prevention strategy that includes the prevention and control of tobacco use as a priority in the reduction of cancer incidence and mortality.

### **EVOLUTION OF THE NCI SMOKING TOBACCO AND CANCER PROGRAMME**

In 1955, the NCI undertook the first large-scale examination of smoking and tobacco use in the USA in conjunction with the US Census Bureau (17). In 1956, the NCI was part of the Surgeon-General's Study Group on Smoking and Health, which issued the first official government statement on smoking and lung cancer (18). When the Surgeon-General's Advisory Committee on Smoking and Health was formed in October 1962, the NCI provided staff and expertise for developing the landmark report on the health consequences of smoking (19).

During the 1960s, the NCI continued its basic biomedical research programme on smoking and tobacco use, expanding its efforts to include studies not only in epidemiology but also of the chemistry, toxicology and pharmacology of tobacco smoke and animal experimentation studies. In the early 1970s, a large-scale effort was initiated to identify hazardous elements in tobacco and tobacco smoke and ways of reducing or eliminating these agents so as to reduce the disease risk of smokers (20). As it became more obvious that a 'less hazardous' cigarette was not a reasonable alternative to prevention and cessation of smoking, the effort changed in the late 1970s to place more emphasis on why people smoke and related behavioural issues.

In 1982, following the publication of the first Surgeon-General's Report that focused entirely on tobacco use and cancer and the enunciation of NCI's goal of reducing cancer mortality rates by up to 50% by the year 2000, the Institute began a major planning effort

to reduce the prevalence of tobacco use in the USA. This programme was entitled the Smoking, Tobacco, and Cancer Programme (STCP).

### **NCI SMOKING, TOBACCO AND CANCER PROGRAMME**

Although the medical and scientific communities had reached consensus on the link between smoking and cancer, there was no consensus on how best to persuade people to give up the habit, or not begin smoking at all. Because of the uncertainties surrounding the effectiveness of specific smoking-control approaches, the NCI initiated a major effort that placed emphasis on the development and testing of prevention and cessation interventions. This highly-focused effort has now become the largest of its kind in the world. Sixty prevention and cessation trials were begun that have affected more than 10 million people in 33 states, eastern Canada, and more than 200 North American communities. The cost of this programme for the years 1982 to 1990 is US\$ 250 million.

The STCP is the focal point of the NCI's disease prevention and health promotion research activities related to tobacco use and cancer. The goal of this programme is to decrease the incidence and mortality of cancers caused by, or related to, smoking and the use of tobacco products. The main thrust for attaining this goal is to develop and apply effective interventions to reduce the prevalence of tobacco use. The STCP's specific objective is to reduce the proportion of adults and youths who smoke to 15% or less by the year 2000.

The priorities for this intervention research effort grew from a systematic planning process that involved state-of-the-art reviews and consensus development, involving hundreds of scientists and public health experts. The result of this planning has been the implementation of a three-step sequence of



activities beginning with the support of nearly 50 large intervention research trials, followed by the controlled application of trial results in a range of communities in North America, leading to a nationwide demonstration project applying all that has been learned in the first two steps of this research-to-applications sequence (Fig. 4).

The steps in this sequence are: (i) intervention research trials; (ii) community intervention trial for smoking cessation; and (iii) American stop smoking intervention study for cancer prevention.

As with all of the NCI prevention and control efforts, it has followed the logic of cancer control phases to determine the nature of readiness to move to the next step in the research sequence (Fig. 5). This logic comprises five sequential phases that emphasize a progression of activity from basic investigations to broad applications in target populations. Between each phase there is a 'decision point' with operational criteria to determine if

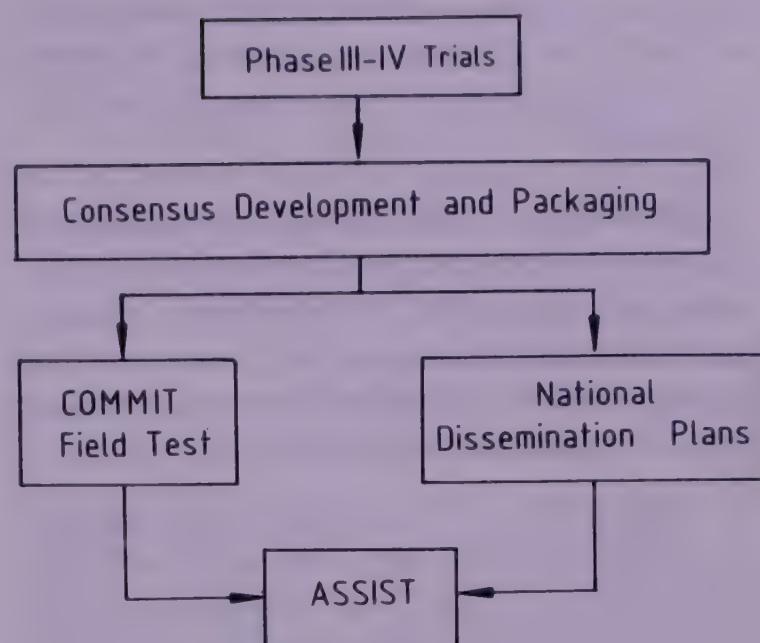


Fig. 4. Model for STCP's research-to-applications of research sequence

research outcomes warrant proceeding to the next phase. This approach is described elsewhere (21,22), but the phases are described briefly below:

**Phase I — Hypothesis development:** In Phase I studies, available scientific evidence

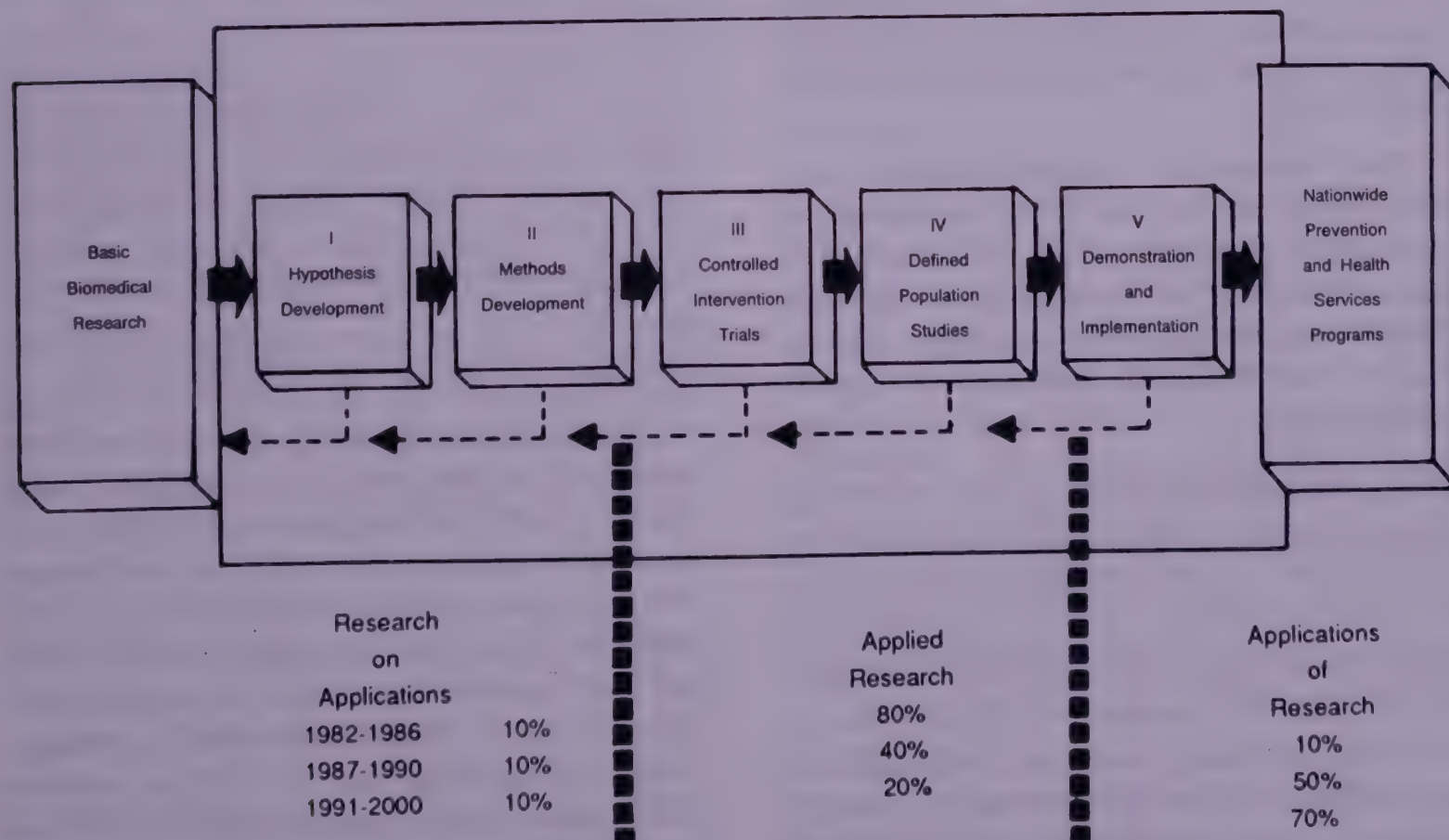


Fig. 5. Cancer control phases applied to the smoking, tobacco and cancer programme



from basic laboratory, clinical, epidemiological and behavioural research is assessed to determine the opportunity for formulating a testable hypothesis.

**Phase II** — Methods development: Phase II studies are designed to characterize the variables to be controlled or monitored in subsequent intervention studies and to ensure that accurate and valid procedures are available before the study is implemented.

**Phase III** — Controlled intervention trials: Phase III trials test the hypotheses developed in Phase I using the methods validated in Phase II. These trials test hypotheses in groups that enable the efficacy of the intervention to be determined.

**Phase IV** — Defined population studies: Phase IV studies are designed to quantify the impact of an effective intervention in a large sample representative of a large target population.

**Phase V** — Demonstration and implementation studies: Phase V demonstrations apply the proven interventions from Phase IV in large communities and measure their public health impact.

The intervention trials' comprise primarily Phase III in the STCP research-to-applications sequence, with a few Phase IV trials; COMMIT is a Phase IV trial; and ASSIST will complete the sequence with a Phase V trial. Each of these steps is briefly described below.

**STCP intervention trials:** After reviewing existing research and consulting with hundreds of experts in relevant fields, the decision was made in 1983 for the STCP to employ a two-part strategy in the development of its intervention trials.

The first strategy involved the design and study of interventions using schools, self-help techniques, physicians/dentists, and the mass media as the means of intervention delivery.

The second strategy targeted specific populations that are at particular risk for tobacco-related cancers and/or are amenable to prevention strategies — youth, minority ethnic groups, women and smokeless tobacco users. These two strategies resulted in eight sets of intervention studies, comprising 49 trials (Table 1).

**Table 1**  
*STCP intervention trials (1984-92)*

Intervention	Number of trials
School-based	10
Self-help strategies	7
By physician/dentist	5
Through mass media	4
Among blacks	7
Among Hispanics	3
Among women	5
Smokeless tobacco use	8
Total	49

The goal of these trials has been to develop cost-effective, durable, generalizable and readily adoptable interventions which can then be field tested in COMMIT and disseminated through ASSIST, the second and third steps in the STCP research-to-applications sequence. The trials were first funded between 1984 and 1987 and will continue through 1992, although many have now begun to report final data and disseminate useful interventions.

In addition to using the interventions developed in these trials in COMMIT and ASSIST, the STCP has prepared summaries of the results and the most effective techniques developed through the school-based (23,24) self-help (25,26) and physician trials (27,28) and has begun to do so with the media trials (29). The target population trials (i.e., women, blacks, Hispanics, and smokeless tobacco users) began later than the others, and their results will be reported as they become available, beginning in late 1990.



**COMMIT — Community intervention trial for smoking cessation:** The Community Intervention Trial for Smoking Cessation (COMMIT) is the largest smoking intervention trial in the world, involving directly or indirectly more than 6.5 million people in the testing of a community-based intervention protocol that can be disseminated nationwide to meet the NCI objective to reduce smoking prevalence by the year 2000. In this trial, the emphasis is on heavy smokers (25 or more cigarettes a day), because of their greater cancer risk and greater difficulty in quitting. Heavy smokers represent only one-quarter of all smokers, but they account for nearly half of all the lung and smoking-related cancers among smokers.

The trial design includes 11 pairs of communities in North America that were matched in size, demographics and location. Following a base-line survey, one community for each pair was selected randomly in 1988 as the intervention site. The primary hypothesis being tested is that the implementation of a defined intervention protocol, delivered through multiple community groups and organizations and using limited external resources, will result in a rate of quitting among heavy smokers that is at least ten percentage points greater (e.g., 25% *versus* 15%) than that observed in the comparison communities.

The COMMIT interventions will build on, coordinate and facilitate community smoking control activities. The overall intervention goals are to: (i) increase the priority of smoking as a public health issue; (ii) improve the community's ability to modify smoking behaviour; (iii) increase the influence of existing policy and economic factors that discourage smoking; and (iv) increase social norms and values that support nonsmoking.

Trial investigators evaluated the STCP intervention trial results, scientific literature and other data sources to define a protocol of

40 required interventions. Examples of these intervention activities are given in Table 2.

As a community trial, COMMIT requires the implementation of a complex intervention protocol in partnership with diverse community organizations and groups. To form this partnership effectively, the protocol required the formation of a community board and task forces in all intervention sites. Following randomization, the process of community mobilization was started so that the community boards could assume the responsibility for planning and managing the protocol implementation. In the 11 sites, the four-year intervention effort will involve more than 1000 physicians, 700 dentists, 1400 worksites, 1000 community organizations, 250 media outlets, 400 schools and 60 cessation service providers.

In addition to COMMIT, of course, major national efforts to deal with the smoking problem in the USA will be continuing on multiple fronts. Social acceptability and public attitudes toward smoking and tobacco use behaviours are changing rapidly. Schools are adopting more effective prevention curricula; worksites are changing policies and encouraging cessation; the health care system is taking a more active role in smoking cessation; and the general population is urging public policy changes related to smoking and tobacco use. As these changing social trends motivate community leaders to take actions, appropriate resources, materials and expertise will be needed to maximize these local efforts. COMMIT will serve as a major laboratory for the study of community-wide smoking cessation and for the evaluation of specific strategies to meet these needs.

**ASSIST — The American stop smoking intervention study for cancer prevention:** One of the major barriers in the effort to control smoking behaviour in the US population over the past 25 years has been the lack of a systematic plan to make practical use of available



**Table 2***Examples of COMMIT intervention activities: trial interventions*

Intervention task force	Public education	Community activities	Policy/economic activities
Health care	Motivate smokers to seek cessation assistance from providers	Physician/dentist/pharmacist training; expand cessation programmes	Seminars/consultation to promote no-smoking policies
Worksites	Promote worksite smoking behavioural changes (presentations, posters, newsletters)	Support worksite cessation programmes (self-help manuals, A/V materials, incentives)	Develop smoke-free worksite policies
Organizations	Presentations at meetings and in organizational media	Promote community cessation resources, self-help programmes of large organizations	Promote smoke-free meetings, organize competitions ('magnet events')
Cessation resources/services	Oral/written information on health consequences, quit resources, maintenance, passive smoking	Counselling, self-help materials, referral to cessation programmes through telephone hotline	Refer to community resources to change policies; information on regional/national smoke-free policies
	Newsletter for smokers/families with information on quit resources through network	Promote self-help, cessation resources, social support through network ('buddy system')	Publicize local smoking policy changes
Public education (media)	'Kickoff', even to publicize other activities; media training for local advocates; local amplification of national events	Self-help information, referrals to cessation resources, including hotline	Publicize policy changes in local institutions, passive smoking issue
Schools	School curricula; student/parent materials; teacher training	Promote parental cessation through youth, combined parent-cessation/adolescent-prevention programmes	Promote smoke-free school policies, sports, other public events. Reduce tobacco sales to teenagers

smoking control technology. During this period, a substantial body of intervention research has emerged from the published literature. With the adoption of ASSIST, NCI and its partner, the American Cancer Society, have committed the resources necessary to ensure the dissemination of this technology to effect large-scale change.

*Rationale and objective:* In 1987, the NCI recognized that as large and as comprehensive as the STCP intervention trials were, they would have little impact on smoking behaviour and even less on cancer mortality rates unless their resulting technology was applied on a national scale. Thus, in April 1987, NCI convened a three-day meeting of more than 250



of the world's most knowledgeable smoking experts to plan the next step in the research-to-applications sequence. It was the group's consensus that many of the STCP strategies being tested were effective and ready to be implemented in a Phase V cancer control research effort.

On the basis of this consensus, the STCP initiated a series of meetings and discussions with experts both inside and outside the programme to plan the approach necessary to affect sufficient numbers of US citizens to achieve the NCI tobacco control objectives for the year 2000. These experts strongly recommended that community-based tobacco control coalitions be established in entire states or in large metropolitan areas in order that at least 50 million Americans be reached in this effort. This recommendation served as the basis for the development of ASSIST.

*Project organization:* ASSIST is a large-scale demonstration project involving entire states and large metropolitan areas. ASSIST sites will be required to form community-based tobacco control coalitions that will be responsible for developing comprehensive tobacco prevention and control plans, and for implementing these plans in a coordinated fashion throughout the demonstration site. State and local health departments, because of their overall responsibility for the public's health, will serve as the fiscal agent for the coalitions; and because of its long history in smoking and health at the national and local levels and its extensive network of local volunteers, the American Cancer Society is a complementary partner whose participation is critical to the success of this project.

The organization of ASSIST is based on a coalition model. The strength of this model is the ability of member agencies to expand smoking control activities within 'existing' systems, to institutionalize smoking interventions for youth, and to initiate and support comprehensive smoking control policies, such as

increasing restrictions on smoking in public places and limiting access to tobacco by minors *via* sales and promotions.

In addition, coalition members will have an institutional agenda that is consistent with smoking control, a network of organization members throughout the demonstration site, an established means of communication, and a structure (or the flexibility to create one) that will support smoking control activities.

*Project implementation:* ASSIST will be implemented in two phases. Phase I, the planning period, started in late 1991 and will last 24 months. Phase II, the implementation period, will begin during 1993 and continue for five years.

During Phase I, each state or metropolitan area coalition will perform a comprehensive site analysis by thoroughly surveying its region to determine the current status of tobacco control and to assess needs. Each coalition will develop a comprehensive tobacco prevention and control plan that not only reflects the unique needs of the ASSIST site, but also meets NCI project standards (based on the Intervention Trials and COMMIT results).

Phase II will involve carrying out the detailed action steps developed during the planning process. NCI standards will set minimum levels of emphasis in different programme areas, including the health care system; workplaces; schools; civic, social and religious organizations; the media; and the social policy arena. Phase II activities will include training health care professionals to deliver cessation services and counselling, provision of targeted cessation interventions in various community locations (particularly worksites), implementation of tobacco use prevention curricula in schools, and involvement of print and electronic media to cover the smoking and health issue more aggressively.



**Evaluation:** Demonstration sites will be evaluated with the assistance of the US Census Bureau. Three surveys are currently planned: a base-line, a mid-project and a post-implementation phase survey. The endpoint of the project is to compare the prevalence of smoking and tobacco use in demonstration sites with that in the rest of the USA. In addition to the census surveys, a number of process and other evaluation studies will be conducted throughout the project.

### **OTHER NCI SMOKING RESEARCH AND CONTROL ACTIVITIES**

While the focus of NCI smoking control activities has been on the intervention trials, COMMIT and ASSIST, these efforts are highly dependent upon the products and results of a number of other smoking-related initiatives within the NCI.

These initiatives include those of the Division of Cancer Etiology in areas such as the mutagenic and carcinogenic effects of various tobacco products and their constituents, the biological and behavioural effects of cigarettes with different yields of nicotine and tar, and the association between exposure to environmental tobacco smoke and lung and cervical cancer in nonsmokers; provision of support for a number of state health departments involved in cancer prevention and control programmes with major tobacco control components (30); studies of involuntary exposure to smoke aboard aircraft (31); efforts to control smoking at work; development of a data bank on tobacco advertising and promotion; adaptation of research results for use by smokers, health professionals and educators (32,33); and many others which help provide the knowledge base for the effort to achieve a smoke-free society.

### **FUTURE SMOKING CONTROL EFFORTS IN THE USA**

Although the NCI experience in control of tobacco use has been the focus here, it is

presented only as a microcosm of the nationwide efforts that have been made and where they will probably go in the near future. Continuing research is certainly necessary, e.g., in such areas as prevention and cessation among minority ethnic smokers, pre-adolescent smoking prevention programmes and cessation programmes for older smokers. The focus of control efforts, however, will more probably be on the dissemination and application of what we already know, as well as on the formulation of policies designed to prevent youth from starting to use tobacco, to help youth and adults who wish to stop to do so, and to protect nonsmokers from the hazards of environmental tobacco smoke.

Disseminating what has been learned about the prevention and cessation of tobacco use as widely as possible and facilitating its use will continue to be the primary focus of many organizations such as the NCI; other groups will expand upon and diversify these efforts. Policy issues such as increased excise taxes on tobacco and earmarking of the proceeds for health promotion activities; limitation of tobacco use in public places; agricultural policy reform; review of tobacco industry advertising and promotion activities; and minors' access to tobacco will all be important and increasingly critical agenda items for the 1990s.

The most crucial aspect of all these issues is that, to achieve optimum success (defined as a smoke-free society by the year 2000), the knowledge gained and the issues to be addressed must be applied in 'a coordinated, complementary fashion'. This is the goal of NCI's ASSIST and should be the goal of any future tobacco use control efforts. If we have learned nothing else in the past decades of research and related activities, it is that single-focus efforts (e.g., media campaigns, school programmes) produce little long-term change in the prevalence of tobacco use. Rather, it has been those efforts which combine a number of coordinated initiatives that



have provided the strongest, longest-lasting reductions in prevalence.

The future of US smoking control efforts, therefore, lies in strengthening existing cooperative relationships among smoking control advocates (e.g., Coalition on Smoking or Health) and facilitating cooperative linkages

among others who have not previously worked together. In this way, with numerous organizations converging on the single issue of reducing tobacco use prevalence with a wide variety of complementary activities, a multiplicative effect is possible and, with it, the realization of a smoke-free society by the end of this century.

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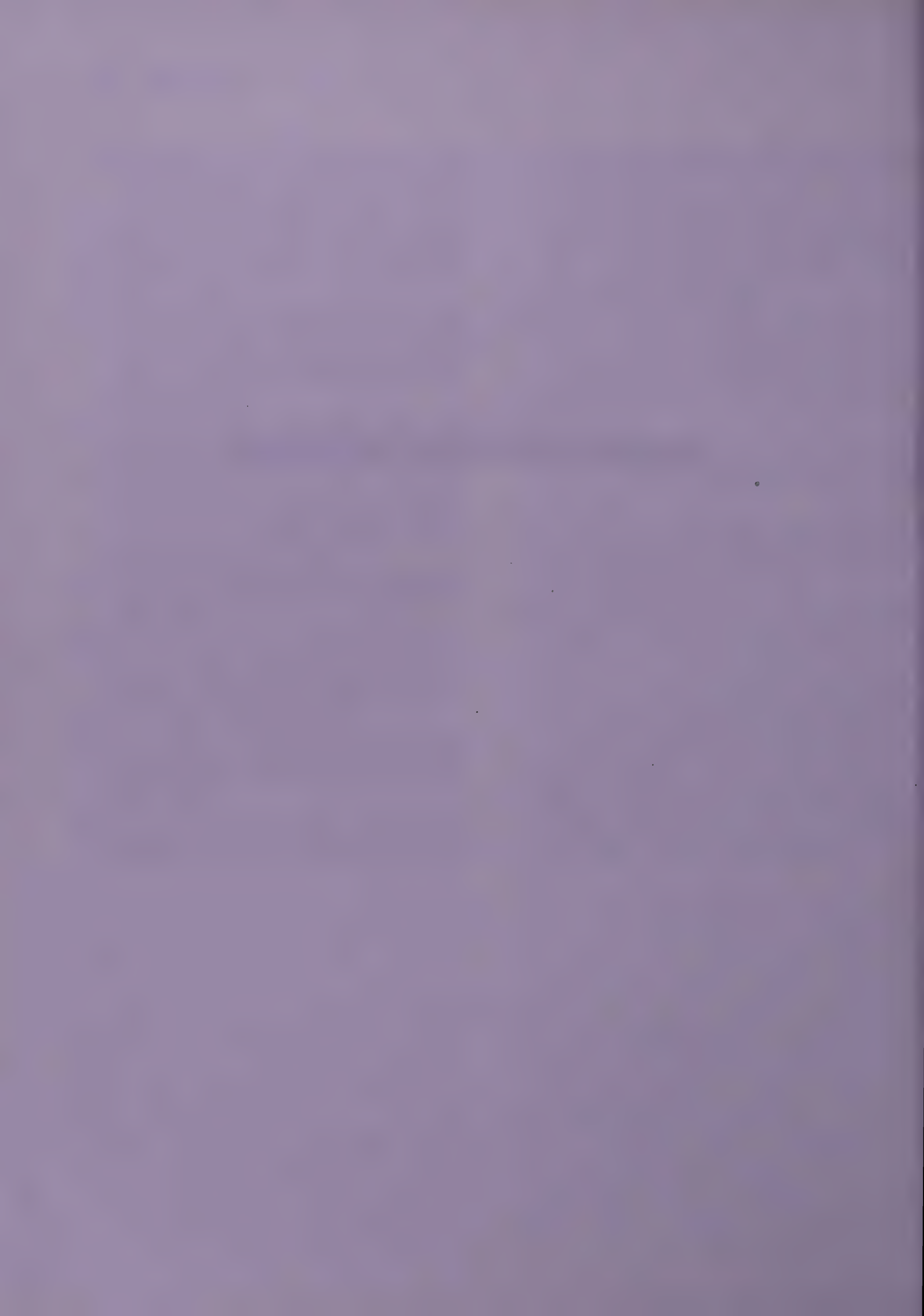
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# **INTERVENTION STUDIES**





# Communication strategies for intervening in the tobacco habits of rural populations in India

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A 10-year prospective intervention study was conducted in three rural areas among 36 000 tobacco users in India with the objective of bringing in behavioural modification and habit cessation. This was a complex exercise, considering that the study population was diverse, illiterate and non-voluntary, coupled with characteristic life styles, beliefs and perceived notions on the medicinal importance of tobacco. In-depth studies and pilot surveys were conducted prior to the planning of intervention. On the basis of these studies, several communication inputs were designed: (i) personal communication, (ii) films, (iii) posters, (iv) folk-drama, (v) radio programmes, (vi) cessation camps, (vii) dental treatment and (viii) newspaper articles. These were pretested and the population was exposed to them in measured doses. These approaches were found suitable and brought about habit cessation in 14% of the tobacco users. Personal communication which afforded one-to-one interaction was the most preferred input by the population.

## INTRODUCTION

Oral cancer is a common cancer in India (1), and voluminous data demonstrate the causal role of tobacco in this disease. It has also been established that tobacco habits are strongly associated with various oral precancerous lesions and conditions, and that oral cancer in most instances originates from precancer (2-5). Motivated by these findings, an intervention trial was undertaken among 36 000 tobacco users in three rural areas in India, namely, Bhavnagar district in the State of Gujarat, Ernakulam district, Kerala, and Srikakulam district, Andhra Pradesh. The broad objectives were to: (i) motivate people to give up their tobacco habits, and (ii) measure its impact on the incidence of oral precancer. This paper describes the planning, design and implementation of communication strategies in pursuance of the first objective of the study.

## STUDY POPULATION

The target population consisted of 12 000 tobacco users aged 15 years and over in each of

the three districts. The tobacco habits prevalent in these areas included smoking cigarettes, *bidis*, *hookli*, *chutta* and reverse *chutta*; tobacco was also chewed by itself, or more often in *pan*, i.e., betel quid. The populations in these areas differed in their life styles, languages, diet, educational level, socio-cultural set-up, attitudes, beliefs and perceptions, and they were non-voluntary.

## PLANNING OF INTERVENTION

The first step in the planning of intervention was to understand the habits — how were they taken up, how they are continued and how they fit into the life style of the habitues — what perceptions they have about the virtues or ill-effects of these habits and finally what will make them quit the habits, if at all.

Very little information was available on the above factors for planning the strategy. Therefore, a series of in-depth interviews with individuals, and short surveys of the population were done in each area. These studies



also investigated what kind of communication inputs the population needed or would be receptive to. These studies showed that although people generally thought that tobacco use is not good, they were not aware of its harmful effects. Accordingly, the focus of the intervention revolved around health education, reinforcement, motivation, suggestion of methods of cessation, and advice on combating withdrawal symptoms.

The following communication strategies were designed, pretested and used with periodic up-dates on the basis of feed-back.

**Personal communication:** Personal communication was provided by examining dentists, social scientists and other members of the team. The type of information to be given by each communicator was predetermined. Personal communication was usually given in a one-to-one or one-to-two ratio and was done with a view to sorting out doubts and learning behaviours that would result in abstention from the habit. The steps in personal communication were worked out in a logical order, keeping in mind the dynamics of human psychology and what it takes for people to make decisions and change their attitudes and behaviour. Visual aids, like pictorial booklets or a set of photographs, were utilized. Personal communication accorded an opportunity for the people to establish trust and confidence so that their individual problems regarding tobacco habits could be discussed. Methods of tobacco cessation and means of combatting withdrawal symptoms were a part of the personal communication.

**Films:** Film is a very powerful medium for creating awareness, especially among non-literate and semi-literate audiences; and when it is utilized effectively, it works in motivating behavioural changes. Its advantage is that it gives information to many people at the same time. Besides giving a uniform message to everyone, it can present information by dramatizing situations that have human appeal.

Two films were produced in local languages specifically for this study. The objective of the first film was to give information and create awareness about the relationship between tobacco habits and oral cancer; the second film was intended to point out how habits are taken up, continued and how they can be given up?

To derive maximum benefit, the film was screened according to a set format. It was shown to small groups at a time; in Kerala, screening was always done in a room, while in Gujarat and Andhra Pradesh this was not always feasible. The screening was preceded by an explanation of the film by social scientists and followed by a group discussion.

**Posters:** Specially designed posters were displayed to serve as a reminder to the target population that they ought to be reconsidering their tobacco habits. Two kinds of posters were utilized, one with a written message and the other with pictures. Slides prepared from these posters were projected in movie houses around the villages. In addition, hand-written posters summarizing the findings in the village were put up.

**Folk-drama:** Plays were produced to correct the prevalent superstitions and misconceptions about tobacco with the objective of discussing and perhaps explaining them. Folk-drama was used in Srikakulam district because *burra katha*, a form of folk-drama with songs and music is popular in this area. The format of *burra katha* was well-suited for conveying intervention messages as it had three characters: the first, a clown represented the viewpoint of the villagers and conveyed their misconceptions and beliefs; the second character represented the examining team, and dispelled the misconceptions; and the third coordinated the information in the right perspective. A special script on tobacco use and oral cancer was written in folk-drama style.

**Radio programmes:** These were utilized to create an environment that would help the



target population to think about their tobacco habits and act as reminders in between examinations. The programmes were made in the form of talks, interviews, dramas, documentaries and spots.

**Cessation camps:** At a particular time, cessation camps were conducted in the villages on request of the target population, who volunteered by saying that they believed what was said about tobacco and would like to give it up but needed help and support. In cessation camps, detailed discussions were held to suggest solutions to the problems of discontinuing the tobacco habits. Regular daily follow-up was maintained for a few days until people felt they could abstain on their own.

**Dental treatment:** Pre-planning surveys revealed that a majority of the people, and most women, began to use tobacco for its perceived medicinal value for tooth-related problems (see paper by Bhonsle *et al.*, this volume). It was decided to address this problem by setting up temporary dental clinics in the villages so as to eliminate at least one of the reasons given for practising the habit. This opportunity was also utilized to conduct exhibitions on tobacco habits and organize group meetings, with a view to encouraging the target population to ask questions and to discuss their feelings and doubts.

**Newspaper articles:** Although literacy was low, with the exception of Ernakulam (65% in 1980), newspaper articles were published in all areas under study to inform and educate people on the subject of oral cancer and intervention. It was hoped that school children and other literate members of the community would read and convey this information.

## METHODOLOGY

The intervention procedures were integrated and matched with routine examinations of the

population. The examinations were done during a base-line survey and 10 annual follow-ups. In each area, oral examinations, interviews and intervention were conducted by a team consisting of dentists, social scientists, interviewers and other supportive personnel. The social scientists were trained in conducting in-depth interviews and in interacting with the population in a considerate and friendly manner. They were also given requisite information on oral cancer and precancer.

The study population in each area was spread over many villages, and the examination procedure lasted 3-10 days in each village, each year. During this period, the social scientists and other members of the team interacted with the population, delivered personal communication, screened the film and fixed the posters.

## EFFECTS OF INTERVENTION

It was gratifying to note that the intervention procedures adopted were easily understood by the villagers and the concept of intervention was well received. This was borne out by the results. For example, in Ernakulam at the end of one year of intervention, 2% had discontinued the habit (6); 9.4% had discontinued after five years (7), 12.3% at the end of eight years (8) and 14% at the end of 10 years (see paper by Gupta *et al.*, this volume). A 'rank ordering' of the inputs by the target population as per their preference indicated that personal communication had been the most helpful to them, perhaps due to the one-to-one interaction that it afforded (9).

## Acknowledgments

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# A 10-year follow-up study for primary prevention of oral cancer among Indian villagers

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Oral cancer is caused by tobacco chewing and smoking. In this behavioural intervention study in Ernakulam district, 12 000 tobacco users were interviewed about their tobacco habits, examined for the presence of oral precancerous lesions and exposed to an intensive programme of health education on tobacco habits. The control cohort was a subset from an earlier study which used a similar methodology but with minimal behavioural intervention. Results after 10 years of follow-up showed that a higher percentage of individuals stopped using tobacco completely in the intervention cohort than in the control cohort. Several other indicators also showed that the intervention had been effective. As a result, the annual incidence of the most common oral precancerous lesion, leukoplakia, decreased substantially in the intervention cohort. Since most oral cancers are known to be preceded by oral precancerous lesions, the results demonstrate that primary prevention of oral cancer is feasible and practicable.

## INTRODUCTION

It is a well-accepted fact that a high incidence of oral cancer in India and in several other South-East Asian countries is caused by the use of tobacco in the form of chewing and smoking. Most of this oral cancer, as much as 90% according to WHO estimates, is directly attributable to the chewing and smoking of tobacco (1). This indicates that oral cancer is amenable to primary prevention. The current study was undertaken to assess the feasibility and effectiveness of a primary prevention programme for oral cancer in a rural Indian population.

In large scale house-to-house cross-sectional surveys of over 150 000 individuals in rural India, the habits of tobacco chewing and smoking were strongly associated with oral cancer and precancer (2,3). A 10-year

follow-up study of 30 000 individuals in three areas showed that all new cases of oral cancer and precancer developed exclusively among tobacco chewers and smokers, although a large proportion of the cohort consisted nonusers of tobacco. In addition all new cases of oral cancers developed among individuals with a prior diagnosis of oral precancerous lesions (4). When tobacco use was stopped or reduced substantially, the regression rates of oral precancerous lesions increased significantly (5). These results establish an almost complete association between tobacco use, oral cancer and precancer.

The present study was undertaken with two objectives: (i) to find out whether individuals in rural areas can be motivated to give up their tobacco habits through a concentrated programme of health education and (ii)



whether this programme would affect the incidence or risk of oral cancer. This study was conducted in three districts of India (see paper by Mehta, this volume) and the results from Ernakulam district in the State of Kerala in southern India where the incidence of oral cancer and precancerous lesions is known to be high, are discussed in this paper.

## MATERIAL AND METHODS

Two distinct cohorts were selected and followed up at annual intervals for 10-years in Ernakulam district. In both cohorts, the base-line and annual follow-ups consisted of an interview and a clinical mouth examination for each individual in house-to-house surveys. In follow-up surveys, each individual was identified before the interview and examination from an alphabetical list of names cross-indexed with addresses and other identifying information.

The commonest method of tobacco smoking was *bidi* smoking and tobacco was chewed most commonly in *pan* (betel quid) (see paper by Bhonsle *et al.*, this volume). The commonest oral precancerous lesion was leukoplakia (see paper by Murti *et al.*, this volume).

The survey teams that went house-to-house consisted of dentists, interviewing clerks, drivers and local help. For the intervention study a social scientist was also a member of the team. The intervention cohort was subjected to a concentrated programme of health education about tobacco use in various different forms (see paper by Aghi *et al.*, this volume), whereas the control cohort was subjected to no such campaign.

**Intervention cohort:** The populations from selected '*karas*' (smallest population unit available through census publications) in Ernakulam district were screened, and all available tobacco users aged 15 years and over were chosen (12 212 individuals) as the study sample. Only temporary residents, very old, sick, infirm or psychologically disturbed

people and those treated for oral cancer were excluded. The base-line survey for this intervention cohort was conducted in 1977-78, and 10 annual follow-ups were conducted thereafter.

**Intervention:** Special studies revealed that many people began to use tobacco and very often continued it because of its perceived medicinal value for disorders such as toothache and gastric disturbances (see paper by Bhonsle *et al.*, this volume). There was almost no awareness of any possible health consequence of tobacco use. The health education programme therefore consisted of two broad categories: (i) information for creating awareness regarding the relationship between tobacco use and oral cancer and convincing the target population of this relationship, and (ii) helping individuals to stop their tobacco use. In the health educational campaign, both personal and mass media communication were employed. For details see the previous paper by Aghi *et al.* in this volume.

The health educational programme was ongoing, dynamic and responsive to feed-back from the target population. All the intervention inputs were pretested before implementation and modified if necessary. The entire health education material was based solely upon scientific facts.

**Control cohort:** For this cohort, '*karas*' were selected by random sampling and the entire population aged 15-years and over was examined. The base-line survey was conducted in 1966-67 and the first follow-up survey three-years later. Eight annual follow-up surveys were conducted, providing 10-year follow-up results. For the purpose of this report, only a subset of the original cohort is included, namely tobacco users in the base-line survey.

**Intervention:** Although health education was not actively attempted in the control cohort, the conduct of the study itself provided some intervention input. The association between oral cancer and tobacco habits was



explained to patients, especially while interviewing and conducting oral examinations. The examining dentists routinely advised patients to give up their tobacco habits, more forcefully if the patient had an oral precancerous lesion.

**Statistical analysis:** The incidence rates of leukoplakia were calculated using person-years method. The numerator for the incidence rate consisted of individuals with a diagnosis of oral leukoplakia in any of the follow-ups, but without a diagnosis of oral leukoplakia, submucous fibrosis or oral cancer in any previous examination. The denominator consisted of person-years of observation among individuals with no prior diagnosis of oral leukoplakia, submucous fibrosis or oral cancer. Variations with time in age and tobacco use were taken into account. Stoppage of tobacco habit was defined as complete discontinuation of any form of tobacco use at least six months prior to the interview.

## RESULTS

Table 1 shows the cohort size and the follow-up details for the intervention and control cohorts. The control cohort was half the size of the intervention cohort. The loss to follow-up was higher in the control cohort (9.9% *vs* 0.9%), and correspondingly follow-up percentages were higher in the intervention cohort.

Figures 1 and 2 show the percentages of men and women who reported stopping of tobacco use at each follow-up in intervention and control cohorts. In the control cohort, there was some variation but no discernible trend. In the intervention cohort, there were very clear, significant, substantial positive trends for both men and women. Among men, the trend was almost constant throughout the 10-year period, whereas among women there was a decrease in the trend after six years.

Table 2 shows the number and percentage of men and women who reported stopping

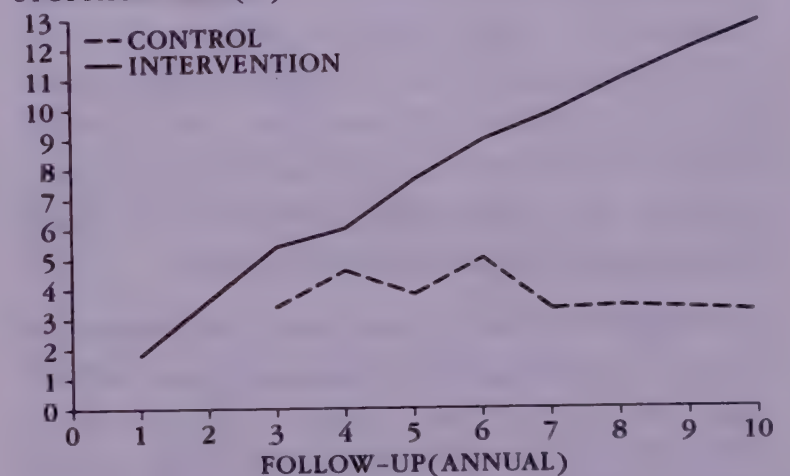
**Table 1**

*Follow-up details after 10 years for intervention and control cohorts*

Follow-up details	Intervention cohort (n=12 212) (%)	Control cohort (n=6075) (%)
Re-examined <sup>a</sup>	93.2-81.2	74.8-71.4
Died <sup>a</sup>	0.7-11.7	2.9-10.3
Maximum followed up	98.4	87.2
Lost to follow-up	0.9	9.9

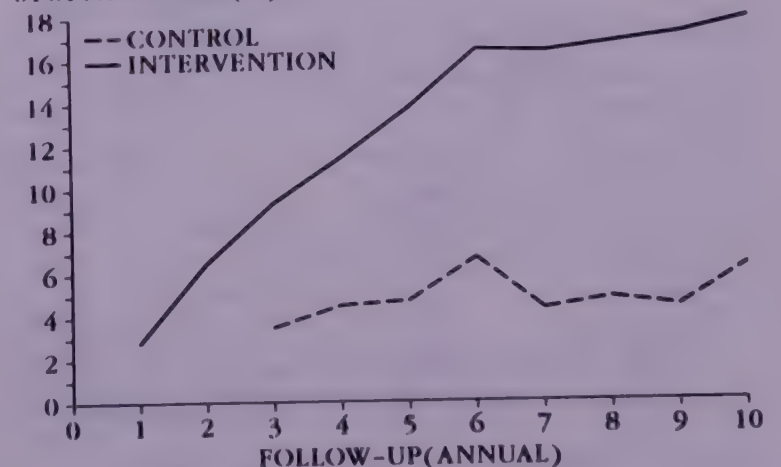
<sup>a</sup>The range is from the first to the last follow-up. The percentage decrease in the individuals re-examined and increase in deaths was fairly steady. The first follow-up of the control cohort was done three years after the base-line survey.

STOPPAGE RATE(%)



**Fig. 1.** Percentages of men reporting stoppage of their tobacco use at each follow-up in the intervention and control cohorts

STOPPAGE RATE(%)



**Fig. 2.** Percentages of women reporting stoppage of their tobacco use at each follow-up in the intervention and control cohorts

**Table 2***Comparison of stoppage of tobacco habit for 2, 3 and 4 successive years in the intervention and control cohorts*

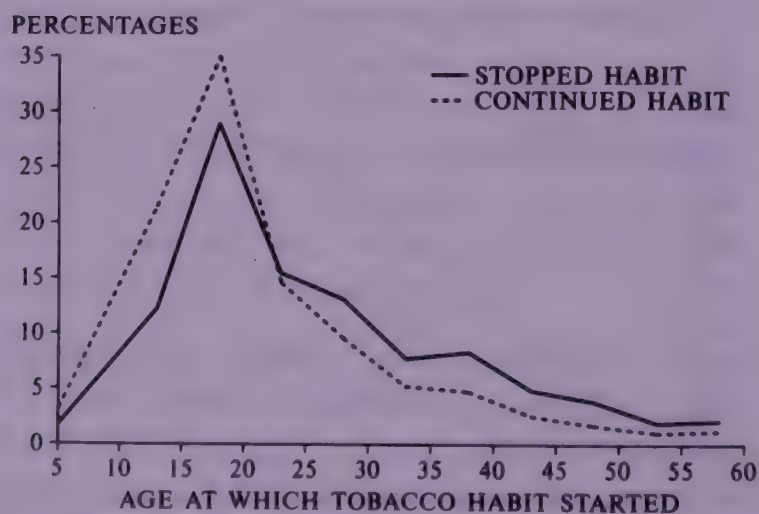
Stoppage	Intervention cohort		Control cohort	
	Followed up No.	Stopped %	Followed up No.	Stopped %
<b>2 years</b>				
Men	8279	11.2	3320	2.2
Women	3466	22.9	1778	7.1
<b>3 years</b>				
Men	8081	8.3	3208	1.7
Women	3391	18.0	1720	5.3
<b>4 years</b>				
Men	7901	6.3	3086	1.0
Women	3336	14.5	1676	4.0

their tobacco habit for two, three, and four consecutive years. These percentages were much higher in the intervention cohort than in the control cohort, showing that more people discontinued their tobacco habit for a longer time in the intervention cohort. The ratios were higher for men than for women.

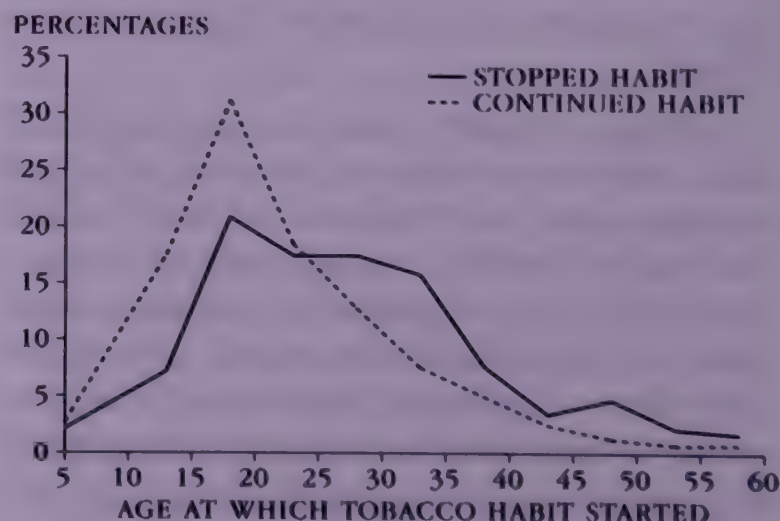
Figures 3 and 4 compare distributions of the age at starting tobacco use of those individuals who stopped their tobacco use and those who did not, in the intervention and control cohorts, respectively. Those who started their

tobacco habit later in life were better able to discontinue than those who started using it earlier. The pattern is similar in both cohorts, but the difference is less pronounced in the intervention cohort.

Figures 5 and 6 compare the distribution of frequency of tobacco smoking per day in the base-line survey and after 10-years in the intervention and control cohorts, respectively. Figures 7 and 8 provide the same information for tobacco chewing. Some individuals in the control cohort did stop tobacco use as indica-



**Fig. 3.** Comparison of distribution of age at starting the tobacco use for those who stopped their tobacco use and those who did not, in the intervention cohort



**Fig. 4.** Comparison of distribution of age at starting the tobacco use for those who stopped their tobacco use and those who did not, in the control cohort



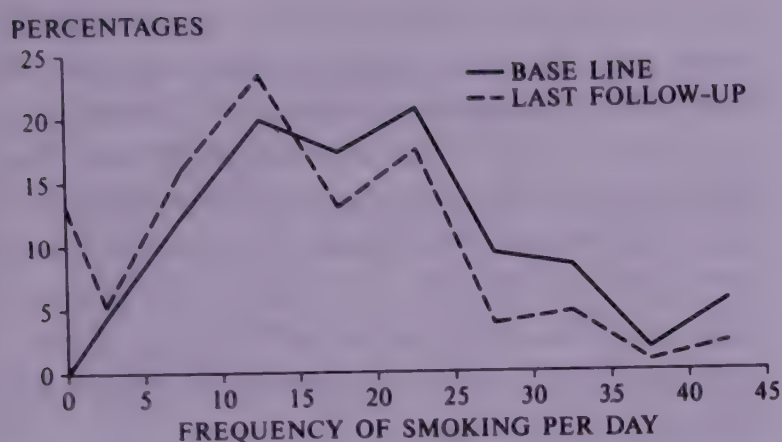


Fig. 5. Distribution of frequency of smoking per day in the base-line and 10th follow-up surveys in the intervention cohort

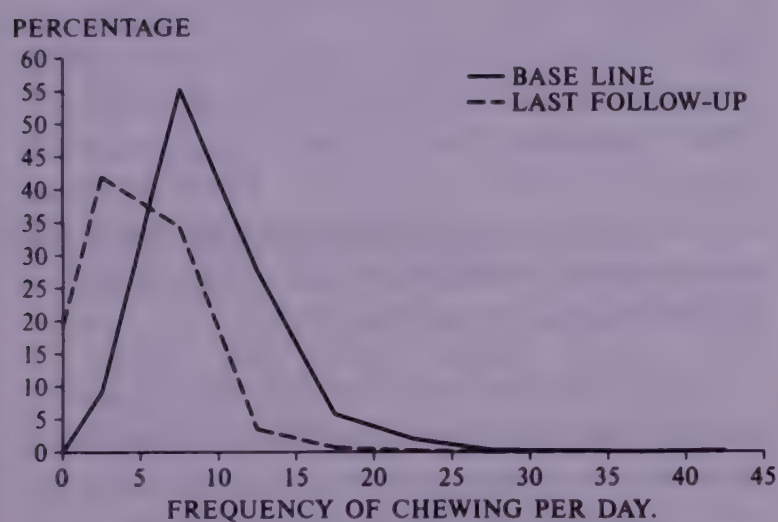


Fig. 7. Distribution of frequency of chewing per day in the base-line and 10th follow-up surveys in the intervention cohort

ted by zero frequency, but there was very little change in the frequency distribution after 10 years. In the intervention cohort, however, not only many more individuals stopped their tobacco habit, but there was a clear and significant shift towards the left for both smokers and chewers, demonstrating that their frequency of tobacco use had decreased.

Table 3 shows the age-specific incidence rates of oral leukoplakia in the intervention and control cohorts. It is clear that the incidence rates in the intervention cohort were substantially lower than in the control cohort.

## DISCUSSION

The results described above corroborate the findings reported earlier after, one, five and

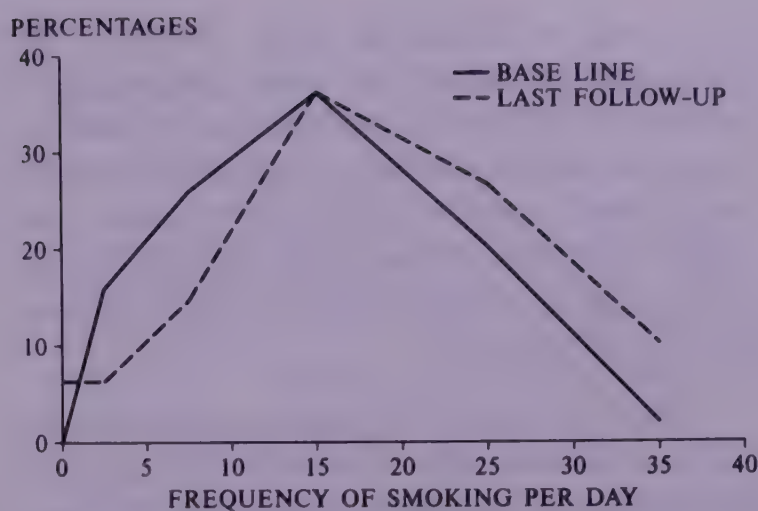


Fig. 6. Distribution of frequency of smoking per day in the base-line and 10th follow-up surveys in the control cohort

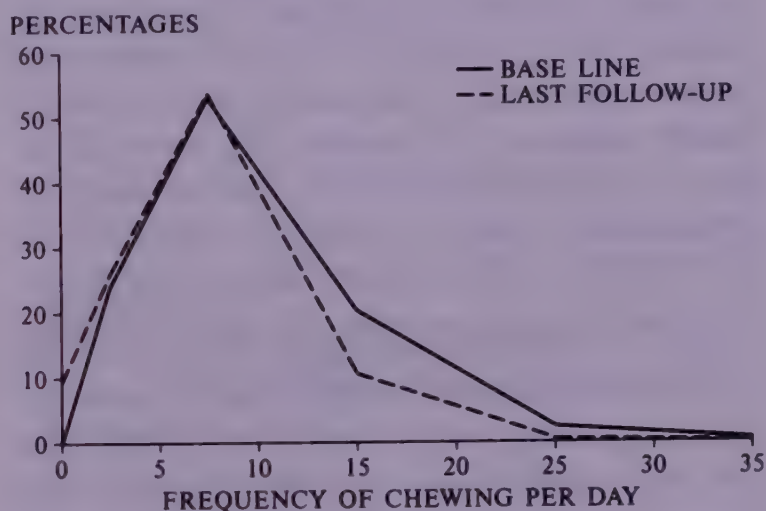


Fig. 8. Distribution of frequency of chewing per day in the base-line and 10th follow-up surveys in the control cohort

Table 3

*Annual age-specific incidence rates (per 100 000) of leukoplakia in the intervention and control cohorts*

Age group (years)	Intervention cohort	Control cohort
<34	77	255
35-44	256	677
45-54	262	846
55-64	373	756
≥65	234	507
Total	236	586
Age adjusted	186	470



eight years of follow-up (6-8). Notably, the percentage of individuals who stopped their tobacco habit in the intervention cohort increased in successive follow-ups. This demonstrates that the effect of health education was cumulative over the years and helped not only in stoppage but even more in continued abstinence from tobacco.

Multiple logistic regression analysis of the five-year follow-up data showed that men who chewed were a difficult subgroup for stoppage of tobacco use, and the educational intervention helped them most (7). Interestingly, the trend in stoppage remained fairly constant for men over the 10-year period, but there was a decrease in the trend for women after six years. Further, this analysis showed that individuals in the higher age groups and those with a shorter duration of tobacco use were more likely to stop their habit. The present analysis demonstrates that it is easier to stop tobacco use if the individual started using it late in life. This confirms and explains the earlier finding.

The objective of the behavioural intervention programme was to stop tobacco use, and this was achieved to a fair degree. The educational programme helped in reducing the frequency of tobacco use in the intervention cohort, and this difference was as much or more pronounced in comparison with the control cohort as the stoppage of tobacco use.

In this study the comparison is not between the intervention and no intervention, but rather between programmed intervention and minimal intervention. It can be hypothesized that in the absence of such minimal intervention, the differences between the intervention and control cohorts would have been more pronounced.

As has already been demonstrated, leukoplakia is the most important oral precancerous

lesion (see paper by Murti *et al.*, this volume), in that it is the most common and is the point of origin for most oral cancers (4,9). Therefore, a decrease in the risk of leukoplakia can be construed as decreasing the risk of oral cancer. This study shows that primary prevention of oral cancer is a feasible and practicable proposition, even among populations who have many misconceptions about the beneficial effects of tobacco.

The study has some limitations. The most important, perhaps, is the non-concurrence of the intervention and control cohorts. In terms of calendar time, the difference between the intervention and control cohort was ten years. Therefore the possibility that the observed differences were due to differences in time trends cannot be entirely ruled out. There is, however, no specific indication that time trend differences exist, or that they affect the validity of the conclusions in any way.

Although the possible benefits of health education in this study have been assessed only in terms of a decrease in the risk of oral cancer, it should be remembered that tobacco use is responsible for increase in the risk of many diseases, such as other cancers, especially those occurring in the aerodigestive tract, heart disease and respiratory disease. It has been estimated that in India tobacco use is responsible for at least 630 000 extra deaths every year (10). Thus, the positive effects of health education would undoubtedly be far greater than simply a decrease in the risk for oral cancer.

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# Epidemiology of tobacco habits in Goa, India

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The Goa Cancer Society has conducted several epidemiological studies in Goa, India, to determine the prevalence of tobacco habits among schoolchildren and adults; to educate schoolchildren through a specially designed school curriculum on tobacco habits and intervention; and to assess the feasibility of using schoolchildren to bring about cessation of tobacco use by their parents or in the community. About 13.4% boys and 9.5% girls used tobacco, mostly smokeless tobacco. Usually, they had begun its use by the age of 5, and generally family members or friends had initiated them to tobacco. Among adults, nearly 33% of men and 20% of women used tobacco; smoking was the most common habit among men, while smokeless tobacco use was most common among women. Schoolchildren who received health education on tobacco and intervention methods were instrumental in achieving stoppage rate of 9.7% among adults. Furthermore, health education imparted a negative attitude to tobacco among the children.

## INTRODUCTION

The State of Goa, which lies on the west coast of India tucked between the states of Maharashtra and Karnataka, became a part of the Indian Union in 1961 after being a Portuguese colony for several hundred years. As in many other parts of India, tobacco use is common in Goa. The prevalence of various types of tobacco habits and the practice of *dhumti* smoking in this area was reported by Bhonsle *et al.* (1).

In Goa, children seem to be a special target for tobacco advertising. Sweets and candies are sold which look exactly like cigarettes and are wrapped in packages similar to cigarette packets (Fig. 1). During the last few years, a tobacco product in paste form, described as 'creamy snuff', has been marketed in toothpaste-like tubes (Fig. 2) under various brand names. Initially, this product is used as a toothpaste; but soon it becomes addictive. Although it costs more than twice a regular toothpaste, its use has become popular.



Fig. 1. Candies that look like cigarettes

Ironically, unlike regular toothpaste, there is no sales tax on this product.

The Goa Cancer Society has undertaken several studies to elucidate the epidemiology of tobacco use in Goa and to explore strategies for



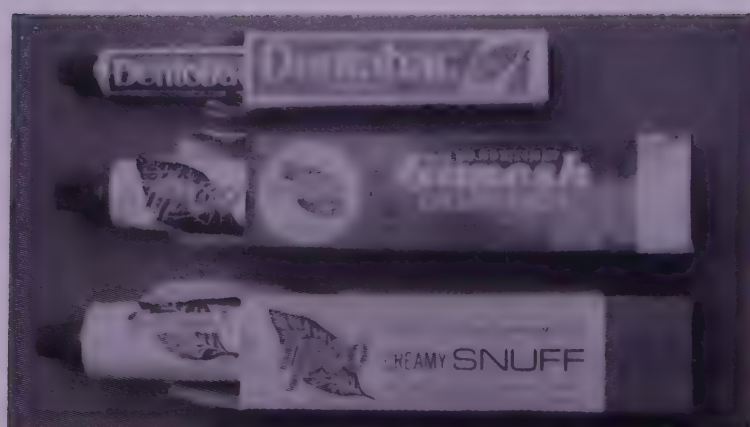


Fig. 2. Creamy snuff in a toothpaste-like tube

effective intervention. Children are considered effective agents for change, particularly in rural India where a school-going child may be the only literate member of the family. In this study, they were educated specifically with a view to conveying intervention messages to their parents.

## MATERIAL AND METHODS

For this study, the State of Goa was divided into three zones: north, central and south, with rural populations of 227 000, 213 000 and 244 000, respectively. The requisite number of villages was selected by random sampling from each zone (21 from the north, 25 from the centre and 27 from the south), from which a population of 50 000 was selected. There were 73 schools in these 73 villages; 31 schools were selected by random sampling, and a questionnaire was distributed to 6271 schoolchildren in grades 5-10. Information was collected on age, gender, kinds of tobacco habits, age at starting those habits and the possible influence of parents and family members on the habit. This survey was done in 1986-87.

In 1987-88, another survey of a total of 29 713 individuals over the age of 15 years in three zones was done through house-to-house visits by selecting a 40% systematic sample from the 73 villages mentioned above. Information on age, gender and details of tobacco used was collected by trained investigators from 10 009, 9801 and 9903 individuals in each zone, respectively.

In 46 selected villages in the north and central zones, education about tobacco habits was given through children. Two booklets, one for 4th and 5th grade students and one for 6th to 9th grade students, were introduced during the academic year 1987-88. These booklets contained information on the history of tobacco, its ill-effects and advice on giving up tobacco habits. Class teachers were given a three-hour course on how to teach this information in four periods, each of 45 min. It was expected that children would not only benefit from this education but would convey the messages to their parents and spread the information in the community. In 25 villages of the central zone, the information was also spread by multi-purpose health workers and *Anganwadi* (child welfare) workers. The remaining 27 villages in the southern zone served as controls.

A sample of 448 boys and 332 girls from the intervention area were re-interviewed and a sample of 432 boys and 289 girls from the non-intervention area were interviewed after two-years to assess the changes in their attitude towards tobacco. These interviews were through self-administered questionnaires.

For the community-based intervention, results are available on 1159 tobacco users in the intervention area of the northern zone and 659 from the control area after about 1.5 years of the base-line survey.

## RESULTS

Tables 1 and 2 give the results from the self-administered questionnaire among 6271 schoolchildren. Tables 3-6 and Fig. 1 give results from a community survey of 29 713 adults. Table 7 assesses the effect of the educational intervention in the community.

Table 1 shows the prevalence of tobacco use according to age and sex among the 6271 schoolchildren. The prevalence was higher (13.4%) among boys than girls (9.5%) and



**Table 1**

*Prevalence of tobacco use according to age and sex among schoolchildren aged 10-18 years*

Age	Boys (%) (n=3443)	Girls (%) (n=2828)	Total (%) (n=6271)
10-14	10.6	9.4	10
15-18	15.4	9.7	12.7
Total	13.4	9.5	11.7

higher in the age group 15-18 years (15.4%) than in the age group 10-14 years (10.6%).

Table 2 shows the types of habits prevalent in the 731 tobacco users among the 6271 schoolchildren. Most (98%) of the boys and girls used tobacco in smokeless form, the commonest being *mishri*, followed by tobacco paste, i.e., creamy snuff, and chewing.

On the question of age at starting tobacco use, the response rate was low: 48% of boys and 52% of girls. Among those who responded, nearly one-third of the 223 boys and one-half of the 152 girls said that they had begun to use tobacco before the age of 5.

The response rate to the question about the people who influenced initiation of tobacco use was also not very high, namely, 62%

**Table 2**

*Prevalence of different types of tobacco habits among schoolchildren*

Habit	Boys		Girls	
	No.	%	No.	%
Smoking	13	3	5	2
<i>Mishri</i>	256	56	177	66
Creamy snuff	212	46	128	47
Chewing	66	14	36	13
Single	388	84	219	81
Multiple	73	16	51	19
Total	461	100	270	100

among boys and 56% among girls. Family members were most influential for initiating tobacco use (boys, 60%; girls, 84%), although among boys other persons like friends (17%) and teachers (10%) were also influential.

Table 3 shows the distribution of the prevalence of tobacco use according to age among 29 713 individuals in the community. About one-third of the men and one-fifth of the women used tobacco. The prevalences increased rapidly up to the age of 44 among men and 64 among women; but prevalence rates among women were almost half of those observed in men up to the age of 44.

**Table 3**

*Prevalence of tobacco habits according to age and sex*

Age (years)	Men		Women	
	No.	Prevalence (%) (n=4778)	No.	Prevalence (%) (n=3152)
15-24	4 815	3.9	4 027	2.3
25-34	2 894	24.6	3 497	11.8
35-44	2 159	49.3	3 043	25.9
45-54	1 952	63.8	2 297	35.4
55-64	1 505	62.7	1 578	41.9
≥65	1 038	53.3	908	42.3
Total	14 363	33.2	15 350	20.5

Table 4 shows the distribution of different types of tobacco use among men and women. Smoking was most common (82.8%) among men, while smokeless tobacco use was most common (67.3%) among women.

**Table 4**

*Distribution of various tobacco habits according to sex*

Habit	Men		Women	
	No.	%	No.	%
Smoking only	3957	82.8	1 031	32.7
Chewing only	217	4.5	1 476	46.9
Mishri only	163	3.4	349	11.1
Creamy snuff	71	1.5	62	2.0
Multiple	370	7.8	234	7.3
Total with habits	4778	100	3 152	100
Total without tobacco habits	9585		12 198	

*Bidi* smoking was the commonest smoking habit among men (63%) as well as women (60.8%). The second commonest smoking habit among men was cigarette smoking (24%), while among women it was *dhumti* smoking (27.3%).

Figure 3 shows the prevalence of tobacco use according to educational level and gender. Tobacco use decreased sharply with increase in the educational level; for example, among men the prevalence was 64% among illiterates, 46% among those with primary education and 14% among those with middle-school education. Among women, it was 38% for illiterates, 11% in those with primary education and 3% among those with middle-school education.

Figure 4 shows the cumulative percentage of men and women starting tobacco use by a given age. Over one-third of individuals started tobacco use before they attained 20 years of age and most of them before they were 30 years old.

Figure 5 shows the reasons for starting tobacco use. About 28% of men started

tobacco use due to a friend's influence and 22% just to pass time. More women started using tobacco either for perceived medicinal

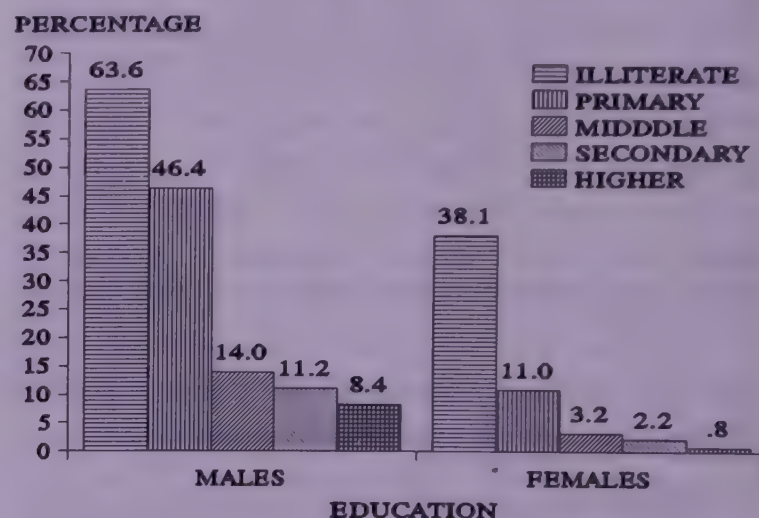


Fig. 3. Tobacco use according to educational level

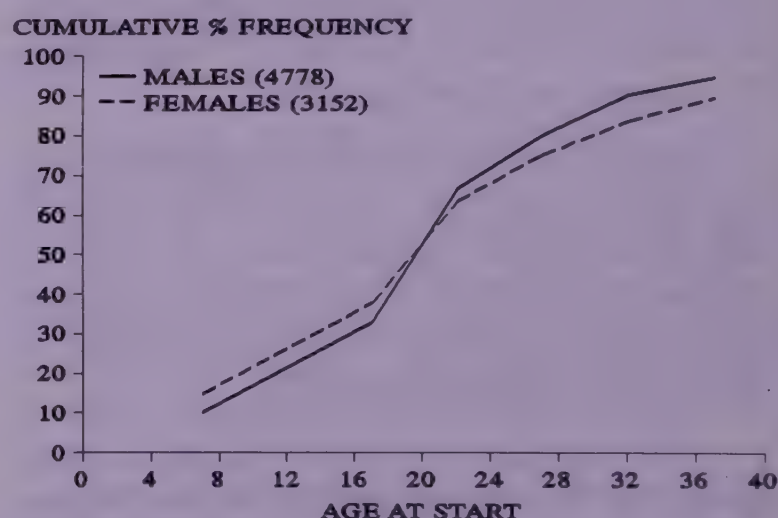


Fig. 4. Age at initiation of tobacco use among adults

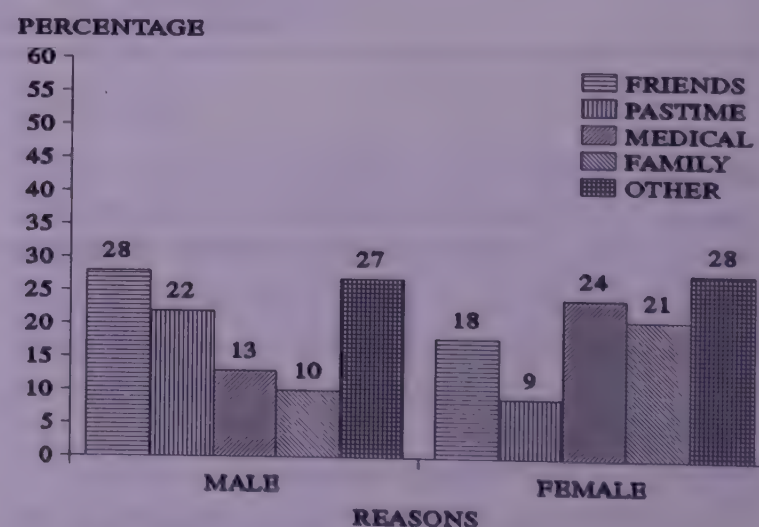


Fig. 5. Reasons for starting tobacco use in a community



**Table 5***Attitude of schoolchildren to the question 'Are you likely to take up tobacco use in future?'*

Attitude	Intervention		Non-intervention	
	Boys (%) (n=448)	Girls (%) (n=332)	Boys (%) (n=432)	Girls (%) (n=289)
Definitely not	80	87	62	65
May not	9	6	14	14
All others	11	7	24	23

 $\chi^2$ Boys=8.2 with df=2 $\chi^2$ Girls=14.9 with df=2**Table 6***Attitude of schoolchildren to the question 'What would you do if a friend/relative offered you a tobacco product?'*

Attitude	Intervention		Non-intervention	
	Boys (%) (n=448)	Girls (%) (n=332)	Boys (%) (n=432)	Girls (%) (n=289)
Definitely refuse and advise	82	89	59	60
Definitely refuse but not advise	10	8	16	15
All others	8	4	27	25

 $\chi^2$ Boys=16.2 with df=2 $\chi^2$ Girls=23.0 with df=2

reasons (24%) or through family influence (21%).

Tables 5 and 6 show the differences in the attitudes of children in schools where educational intervention was performed after about two years, compared to those in schools where there was no intervention. The attitudes were determined by analysing responses to two questions: 'Are you likely to take up tobacco use in future?' (Table 5) and 'What would you do if your friend/relative offered you a tobacco product?' (Table 6). Although answers were given on five-point and six-point scales, respectively, they are presented in the tables, in terms of three categories by combining all extremes due to small numbers. For both questions, the difference between intervention and

non-intervention schools was significant for boys as well as girls ( $p < 0.001$ ).

**Table 7***Rates of stopping tobacco habits among men and women*

Cohort	Men	Women	Total
<b>Intervention</b>			
Followed-up	705	454	1159
Quit	63 (8.9%)	50 (11%)	113 (9.7%)
<b>Control</b>			
Followed-up	378	281	659
Quit	24 (6.3%)	16 (5.7%)	40 (6.1%)

Table 7 shows rates of stopping tobacco use in the intervention and control areas in the community according to gender. Overall, a significantly higher percentage (9.7%) of men and women stopped their tobacco use in the intervention area compared with the control area. The difference was significant for women, but not for men.

## DISCUSSION

This investigation showed that tobacco use in different forms is very common in Goa and its use generally starts at a very young age, mostly influenced by family members and friends. The finding that smoking is the most common habit among men and tobacco chewing is more often practised by women is similar to that of an earlier study in this region (1) and of studies in other parts of India (2). The present findings are also consistent with those of

studies (3-5) in other parts of the country: that it is possible to motivate people in rural areas of India to quit their tobacco habits (see paper by Gupta *et al.*, this volume). Furthermore, the present investigation focused on the importance of desirability of including health educational material on tobacco in school curricula. It highlights the findings that such material is useful in shaping the children's attitude towards tobacco in a proper perspective and in propagating the intervention messages to their parents.

## Acknowledgments

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## **POLICY AND LAW**





# Impact of cigarette advertising revenues on US magazine coverage of smoking and health

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The belief that US magazines have restricted their coverage of smoking and health to avoid offending the cigarette companies has been investigated in a scientifically rigorous manner. Four secondary data sources were employed to collect annual data on 99 magazines over a period of 25 years. With the unit of analysis being a magazine in a given year, we used logit regression analysis to test whether magazines' coverage of smoking and health was related to their advertising revenue. Controlling for their size of readership, the demographics of their readers, and their propensity to cover health topics in general, we found that the probability of a magazine covering smoking and health is statistically significantly negatively related to its dependence on cigarette advertisements as a source of revenue.

## INTRODUCTION

Cigarette advertising is a major economic enterprise in the USA. In 1988, US cigarette manufacturers spent US\$ 3.3 billion on cigarette advertising and promotion (1), equivalent to US\$ 13 for every man, woman and child in this society, or almost US\$ 65 for every smoker. In recent years, cigarette advertising has accounted for more than 10% of all advertising revenues in US magazines (2). Currently, the tobacco companies spend in the vicinity of US\$ 300 million per year on magazine advertisements.

Within the public health community, there is a strong perception that magazines have restricted their coverage of the hazards of smoking for fear of offending cigarette advertisers. If this perception is true, there is a logical train of thought that leads to the conclusion that restriction of coverage is responsible for additional smoking and, hence, additional cancer and other illnesses due to smoking. This train of thought runs as follows: reduced coverage of smoking means that readers are less well

informed about its hazards than they would be if coverage were defined exclusively by the inherent interest and importance of the subject to health. Because readers are less informed, they have a reduced perception of the risk of smoking. This reduced perception of risk, in turn, results in more smoking than would occur if there were a full and open discussion of the hazards of smoking. Finally, more smoking induces more morbidity and mortality.

In the remainder of this paper, we describe the nature of the evidence that supports the belief of the public health community that magazines censor their coverage of the hazards of smoking. First, we describe the nature of the evidence that existed until our recent work on the subject. Then, we describe the new work. Finally, we discuss the implications of our findings, combined with previous evidence, to the international situation with regard to smoking and health.

## EVIDENCE TO DATE

Evidence about the phenomenon of self-censorship has been largely anecdotal, although



a few simple correlation studies bolster the belief that the phenomenon is real. Many of the anecdotes reflect authors' reports that their discussions of the hazards of smoking have been removed from articles on, for example, avoiding cancer (3). Occasionally, authors have reported that articles that were initially accepted were not published once the issue of smoking was raised. At the other extreme, tobacco companies have withdrawn advertising from magazines that have run articles on the hazards of smoking. A prominent example occurred in the late 1970s in the case of 'Mother Jones' (3). The literature describing such anecdotes has been reviewed previously by the senior author (4,5).

The episode that galvanized the public health community on the issue of the self-censorship of magazines regarding smoking was the publication by 'Newsweek' in 1983 of a special supplement entitled 'Personal Health Care'. Written by the American Medical Association (AMA), the supplement promised to inform readers about the most important information needed to protect their health. The supplement included 16 pages of detailed advice on such subjects as diet, nutrition and exercise; the text included only four sentences on smoking, not one of which said that the behaviour was hazardous to health. The same issue of 'Newsweek' had 12 pages of cigarette ads worth approximately US\$ 1 million in revenues to the magazine. While 'Newsweek' and the AMA offered excuses for the absence of the discussion of the hazards of smoking, the apparent truth of the matter was revealed in a letter from the 'science news editor' of the AMA to a physician in the State of Washington. The editor wrote, "Newsweek resisted any mention of cigarettes" (4).

This episode was followed a year later by another supplement, this one in 'Time' magazine, written by the American Academy of Family Physicians. This supplement included no mention of smoking in its entire text, including only a single reference to smoking in

bed in a health quiz. The same issue of 'Time' included eight pages of cigarette ads. The Chairman of the Board of the Academy later acknowledged that 'Time's editors had removed discussion of smoking from each successive draft of the supplement (4).

Such anecdotal evidence on magazine self-censorship has been bolstered by several non-random, simple correlation studies. In the first of these, the American Council on Science and Health examined 10 prominent women's magazines that carried cigarette ads and two that did not. Between 1967 and 1979, the 10 magazines that carried cigarette ads produced a total of eight feature articles that seriously discussed quitting or the dangers of smoking. This amounted to less than one article per magazine per decade. By contrast, 'Good Housekeeping', which does not accept cigarette ads, had 11 articles on the subject, more than the total of the other 10 magazines combined. 'Seventeen', which also refuses cigarette ads, had five stories on the hazards of smoking during that period. The authors of this study noted that the magazines that accepted cigarette ads had up to 63 times as many articles on other health topics, specifically including nutrition, contraception, stress and mental health. In 'Good Housekeeping' and 'Seventeen', by contrast, the subject of smoking received much more balanced treatment (3).

In a second study, the American Council on Science and Health looked at the coverage of smoking and the proportionate share of cigarette advertising in magazines that had published a minimum of 60 articles on health between the years 1965 and 1981. Table 1, taken from that study, shows the relationship between cigarette advertising and coverage of smoking in these magazines. The three magazines that provided the most substantial coverage of smoking ('Reader's Digest', 'Good Housekeeping' and 'Prevention') did not receive any cigarette advertising revenues. Of those magazines that did publish cigarette ads,



**Table 1**

*Cigarette advertising revenues and coverage of smoking and health; selected magazines including 60 or more health-related articles, 1965-81<sup>a</sup>*

Magazine	% of health articles discussing smoking	Cig. ad revenues as % of total ad revenues
<i>Reader's Digest</i>	34.4	0
<i>Good Housekeeping</i>	22.1	0
<i>Prevention</i>	15.4	0
<i>Vogue</i>	11.7	5.1
<i>US News &amp; World Report</i>	7.4	14.6
<i>Ladies' Home Journal</i>	7.1	16.3
<i>Time</i>	6.9	17.2
<i>Harper's Bazaar</i>	4.5	7.1
<i>McCall's</i>	4.5	15.1
<i>Newsweek</i>	2.9	15.8
<i>Cosmopolitan</i>	2.3	9.4
<i>Mademoiselle</i>	1.9	7.3
<i>Ms.</i>	0	14.8
<i>Redbook</i>	0	16.1

<sup>a</sup>Source: ref. (6)

only one, 'Vogue', mentioned smoking in as many as one out of 10 of its health articles, and it had the lowest percentage of cigarette advertising of any of the other magazines seen in the table (6). At the same time, there is no obvious correlation between the amount of advertising and the amount of coverage accorded to smoking issues in the magazines that accepted advertising. The principal observation derived from these data is that the only magazines that provided substantial coverage of the hazards of smoking were those that did not accept cigarette advertising.

### A NEW STATISTICAL ANALYSIS OF THE RELATIONSHIP BETWEEN CIGARETTE ADVERTISING AND COVERAGE OF SMOKING AND HEALTH

The correlational evidence cited above is highly suggestive. But because it comes from a

relatively small sample of magazines, and does not control for additional variables that might influence the coverage of smoking, we decided to undertake a more comprehensive study. Utilizing four major data sources (Table 2), we collected data on 99 magazines for the years 1959-86 (excluding 1970-72). The data set includes information on cigarette and total advertising revenues, coverage of smoking and health and 18 additional health risk factors, readership characteristics, circulation and type of magazine.

In a preliminary study, we examined changes in coverage of smoking and health in 50 magazines that had either included or excluded cigarette ads through most of this period. We compared ad revenues and coverage of smoking and health before and after the ban on broadcast advertising of cigarettes, which took effect in 1971. The ban led to a dramatic increase in advertising dollars received by magazines (Table 3). As can be seen, in the 39 magazines that included cigarette advertising both before and after the ad ban, total

**Table 2**

*Major data sources, empirical analysis of the relationship between cigarette advertising revenues and coverage of smoking and health, 99 US magazines, 1959-86<sup>a</sup>*

Source	Data provided
Magazine index	Computerized indexing of subjects covered in articles in 435 US magazines, 1959-86 (excluding 1970-72)
Leading national advertisers/publishers information bureau	Advertising pages and revenues by product category, for approximately 150 US magazines, per issue, quarter and year
Audit bureau of circulation	Number of subscriptions, paid and unpaid
Simmons market research bureau	Readership demographics, including distributions by age, sex, race, income and education

<sup>a</sup>Source: ref. (7)



**Table 3***Advertising revenues in 39 magazines with cigarette ads<sup>a</sup>*

Years	Cigarette ads  (1983 US\$, millions)	Total ads	Cigarette ads as % of total
1959-69	326	17 310	1.9
1973-83	2697	24 556	11.0
Percent change	+727	+42	+479

<sup>a</sup>Source: ref. (2)

advertising rose by 42% in constant 1983 dollars, but cigarette advertising rose by a phenomenal 727%. In the 11 years prior to the ad ban, 1959-69, cigarette ads constituted 1.9% of total advertising revenue in these magazines. From 1973-83, however, cigarette ads leapt to 11% of the total (2).

During the same period, coverage of smoking and health in the 39 magazines that accepted cigarette ads fell by nearly two-thirds (Table 4). Among the 11 magazines studied that did not publish cigarette ads throughout those periods, coverage fell by 29%. Some of the reduction in coverage in both groups of magazines might reflect a decrease in the salience of the smoking and health issue as a newsworthy topic. As a check on this possibility, we examined the change in coverage of smoking

**Table 4***Number of articles on hazards of smoking in magazines with and without cigarette ads<sup>a</sup>*

Years	No. of articles			
	Magazines with cig. ads (n=39)	Magazines without cig. ads (n=11)	New York Times	Christian Science Monitor
1959-69	137	38	1301	271
1973-83	48	27	1023	262
Percent change	-65	-29	-21	-3

<sup>a</sup>Source: ref. (2)

and health in two major newspapers for which subject indices were available, 'The New York Times', and the 'Christian Science Monitor'. The 'Times', like most newspapers, derives only a small percentage of its advertising revenues from cigarettes (on the order of 1 or 2%), while the 'Monitor' does not accept cigarette advertising. In 'The New York Times', coverage decreased from the first to the second period by 21%, a figure that was statistically significantly lower than the decrease in the magazines with cigarette ads, but not statistically different from coverage in the magazines that did not have cigarette ads. The 'Christian Science Monitor's coverage dropped by only 3%, a statistically significantly smaller decrease than that of 'The New York Times' (2).

This preliminary study led to a more sophisticated regression analysis of the data. Described in another paper (7), this analysis involved examining the hypothesis of an association between dependence on cigarette advertising and coverage of the hazards of smoking, from two perspectives. First, we tested whether the fact of any acceptance of cigarette advertising decreases the probability of a magazine's covering smoking issues during a given year. Second, we assessed whether a magazine's relative dependence on cigarette advertising (as measured by the proportionate share of cigarette ads in total advertising) affected the probability of covering smoking and health issues.

Using a dichotomous dependent variable, namely whether or not a magazine covered smoking and health in a given year, we employed logit regression analysis to assess the relationship between cigarette advertising and coverage of smoking and health issues. Our control variables included an index of coverage of other major health risk factors; a dummy variable for the year 1964, the year of the first Surgeon-General's Report on Smoking and Health (8), a document whose release received an extraordinary amount of press coverage (9);



dummy variables for the decades of the 1970s and 1980s, reflecting the overall shift in ad dollars from the broadcast media to magazines; a dummy variable indicating whether a magazine was a news magazine, which would be expected to provide more coverage of smoking and health than other magazines; a dummy variable indicating whether a magazine was a women's magazine; and an interaction term between the measure of cigarette advertising and the fact of a magazine being a women's magazine. The last two variables were included to investigate the common belief that women's magazines have been particularly susceptible to the self-censorship phenomenon (3,5).

Because the estimated coefficients from the simple logit regression could reflect magazine effects (i.e., time invariant characteristics of individual magazines that are not included in the model), we regressed a means-differenced model. The relationships observed in the simple logit regressions held. Similarly, to test for autocorrelation, we regressed the residuals on their lagged values. This revealed no autocorrelation.

As we report elsewhere (7), the results of our study support the conventional wisdom that there is a significant inverse relationship between cigarette advertising and coverage of the hazards of smoking. Our findings added a different wrinkle to the conventional wisdom, however. We did not find support for the hypothesis that the mere presence of any cigarette advertising influenced the probability of covering smoking and health, although we did find this fact to hold true specifically for women's magazines. We did find, however, that there was a statistically significant negative relationship between a magazine's probability of covering smoking and health and the proportion of the magazine's advertising revenues attributable to cigarette advertising. Again, we controlled for the magazines' propensity to cover health in general, as well as the other variables. The relationship between the

proportion of cigarette ad dollars and coverage of smoking and health issues was particularly strong in the case of women's magazines.

## IMPLICATIONS

Our new work adds strong evidence to the conventional wisdom that cigarette advertising in magazines is associated with diminished coverage of the hazards of smoking. The possible implications of this finding have been discussed in the 'Introduction' to this paper. Particularly noteworthy, in light of the international interests of this Symposium, is the importance of this phenomenon in the case of the developing countries, especially those that are, or will become, targets of the transnational tobacco companies. There is substantial evidence that when the transnational tobacco companies move into a country, the volume of cigarette advertising increases rapidly (10). For example, when Japan was forced by the Office of US Trade Representative to decrease its barriers to the importation of US cigarettes, cigarette advertising on Japanese television went from a negligible amount to the second most substantial source of advertising revenues on the airwaves.

Just when smoking is being aggressively marketed to people who are not well-informed about the health effects of smoking, as is the case throughout the developing world, it is likely that the media will feel increasingly restrained from providing these people with the full information they need to make a rational decision about smoking. Cigarette advertising, it appears, may compromise the true freedom of the press. As disturbing as that would be in its own right, it is particularly disturbing when the implications are measured in thousands of additional deaths.

## Acknowledgments

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# Tobacco policy: the power of law

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While public education has been acknowledged to be important in increasing the social unacceptability of smoking, it is not sufficient to control tobacco use. It needs to be supplemented and potentiated by legislation and the power of law. We have refined our knowledge about the precise functions of legislation in control of tobacco use, options for legislation, suitable ways to implement laws, the impact and effectiveness of different kinds of legislation, priorities for enacting legislation, and general strategies for developing sound public policy. Legislation can bring forth the benefits of scientific knowledge to protect the health of the people and can create leverage for health promotion and form a basis for imaginative programmes to control smoking.

## INTRODUCTION

Experience over the past few decades in combating the smoking epidemic has taught us a number of lessons. The principal lesson, I submit, is that legislation is an essential underpinning for educational and cessation programmes on tobacco use. This lesson was set forth as early as 1983 when a WHO Expert Committee on Smoking Control Strategies in Developing Countries said: "It may be tempting to try introducing smoking control programmes without a legislative component, in the hope that relatively inoffensive activity of this nature will placate those concerned with public health, while generating no real opposition from cigarette manufacturers. This approach, however, is not likely to succeed. A genuine broadly defined education programme, aimed at reducing smoking must be complemented by legislation and restrictive measures..."(1).

This message was reinforced by Warner with historical experience (2). He pointed out that while public education has been vitally important in increasing the social unacceptability of smoking, 'the battlefield has shifted to the public policy arena'. In short,

experience has shown that education is a necessary, but not a sufficient, condition for control of tobacco use. To supplement and to potentiate public education, we need legislation and the power of law.

In addition to this over-arching lesson on the importance of legislation, we have refined our knowledge about; (i) the precise functions of legislation in control of tobacco use; (ii) options for legislation; (iii) suitable ways to implement laws; (iv) the impact and effectiveness of different kinds of legislation; (v) priorities for enacting legislation; and (vi) general strategies for developing sound public policy. My plan is to examine these issues in a series of questions and answers.

## WHY ENACT LEGISLATION?

Legislation is a powerful tool for closing the gap between scientific knowledge and public policy. Translating scientific discoveries into programmes that bring the benefits of scientific findings to people involves, first, dissemination of that knowledge and, second, legislation to establish public policy.

The specific purposes of legislation to control smoking are to: (i) set forth governmental



policy on production, promotion and use of tobacco; (ii) encourage smokers to stop smoking and to dissuade potential smokers, particularly young people, from starting to smoke; (iii) protect the right of nonsmokers to breathe clean air; (iv) reduce to some extent the harmful substances in cigarettes; (v) contribute to the development of a social climate in which smoking is unacceptable; and (vi) provide the basis for allocating resources to support effective programmes to combat smoking.

It is true that voluntary agreements between governments and the tobacco industry in Denmark, New Zealand and the United Kingdom have achieved certain limited restrictions on advertising, health warnings on cigarette packages and publication of tar and nicotine contents of cigarettes, but these agreements have proven to be inadequate, difficult to monitor and enforce, and generally weak instruments for combatting the smoking epidemic. In India, a voluntary agreement between the Indian Government and the tobacco industry prohibits advertising on television and radio. These agreements, however, leave the industry free to evade the intent of the restrictions through billboard advertising and sponsorship of sports and cultural events (3,4). The Royal College of Physicians London has repeatedly urged the British Government to replace the voluntary agreement with legislation, and similar efforts are being made in Denmark and New Zealand.

Evidence that the legislative approach, rather than the voluntary agreement, is effective comes from several sources. Here only two are mentioned. In a 1984 study, researchers in the United Kingdom analysed data from 15 countries between 1962 and 1980 and concluded that countries with legislative programmes made substantially more progress in containing and reducing smoking levels than countries with voluntary agreements (5). Additional evidence comes from comparing

Norway, which has strong antitobacco legislation, with the United Kingdom, which relies on its voluntary agreement with the industry. In 1984, the *per-caput* consumption of cigarettes in Norway corresponded with the low consumption in the United Kingdom in 1954 and the lung cancer death rate for males aged 60-90 in the United Kingdom was more than three times that of the comparative Norwegian rate (6). The truth of the statement of the WHO Expert Committee that effective smoking control programmes require a legislative component has been definitely established.

### WHAT OPTIONS FOR LEGISLATION EXIST?

Three basic approaches to enacting legislation in a country are available: (i) a single-faceted, categorical law, such as the 1975 statute of India requiring health warnings on cigarette packages and on advertisements (7); (ii) a multifaceted statute with several legislative strategies, such as the legislation of Hong Kong, requiring health warnings and tar group designations on cigarette packages and advertisements and prohibiting smoking in specific public places (8); or (iii) a comprehensive statute covering many strategies, including tax and price increases as well as allocation of tax revenues for education about tobacco and health. Finland (9), Norway (10) and Iceland (11) have enacted such laws.

Critical to the choice among these three types of legislation are: (i) political will that policymakers in a particular country have to act on the problem of tobacco and health; and (ii) the knowledge and concern of the people about the ravages of tobacco use and the dangers of passive smoking.

In addition to differences in the scope of legislation, there may be differences in the level of government at which antitobacco legislation is enacted. Choice of the level of government for enacting legislation depends on the legal



powers of the national government and of sub-national governmental units, on legislative traditions, and on political feasibility. National legislation has the advantage of providing a powerful, overall thrust and of protecting the total population. But, in many instances, it is preferable or more feasible to enact legislation at the state or even at the local level of government.

In India, where health legislation is generally a function of the states, only major issues of great importance requiring uniformity throughout this vast country command federal action, as in the case of mental health legislation or health warnings on cigarettes. In the USA, also, the states have great power to enact health legislation under the inherent police power of the states. Federal legislation on tobacco has until now been quite limited. Federal legislation in the USA bans advertising on the electronic media, requires strong, rotating health warnings, and now prohibits smoking on virtually all commercial domestic flights. But many states have enacted state-wide clean indoor air acts banning smoking in public places, and local ordinances have been surprisingly successful in accommodating the rights of smokers and nonsmokers in the workplace. Senator Edward Kennedy recently introduced in the US Congress comprehensive national legislation calling for US\$ 185 million to be spent on regulation of tobacco, anti-smoking advertising and research and prevention programmes, so that Federal legislation may be more powerful in the future.

What, then, are the specific types of legislation that are available? Legislation to control tobacco use may be divided into two broad categories: (i) legislation designed to bring about changes in the production, manufacture, promotion and sale of tobacco; that is, legislation on the production or supply side; and (ii) legislation designed to promote changes in smoking practices or behaviour; that is, legislation on the consumption or demand side.

## WHAT ARE THE FEATURES OF VARIOUS TYPES OF LEGISLATION TO CONTROL PRODUCTION, SALE AND PROMOTION OF TOBACCO?

**Control of advertising:** The tobacco industry spent US\$ 3.3 billion in 1988 on advertising in the USA to lure consumers to its products. By associating smoking with youth, sports, beauty in nature, and sex, the industry creates the illusion that smoking is a pleasurable, healthful and sophisticated activity.

Recently, the industry embarked on a bold and shocking campaign in the USA to use the Bill of Rights to promote its lethal product. Philip Morris paid the US National Archives US\$ 600 000 for the right to use the Bill of Rights on television, radio, print advertisements and other promotional materials, and the National Archives agreed to use its best efforts to secure for Philip Morris the right to use the voices of former Presidents and other leaders, such as Martin Luther King, Jr (12). Already, large advertisements, blazoning quotations about the Bill of Rights, are appearing in newspapers to create a climate of opinion opposed to the restrictions on tobacco advertising that are pending in Congress.

Control of advertising is the most common type of smoking control legislation. As of 1991, 104 countries in the world had enacted controls on advertising. These controls are of varying degrees of stringency (13). Twenty-seven countries have total bans. Seventy-seven countries have strong partial bans restricting the contents of advertisements, the places where advertising is permitted, and promotional activities, or moderate partial bans. The trend is towards stronger laws, as countries amend their limited laws to provide ever stronger restrictions.

Experience with different kinds of restrictions on advertising has taught us several lessons. They are: (i) the stronger the restriction the more effective is the legislation; (ii) it is important to require visible, strong health



warnings on all advertisements; and (iii) it is essential to ban all sponsorship of sports and cultural events and to prohibit association of tobacco with other products. The industry seeks and finds any loophole in the legislation, any chink in the armour of laws restricting advertising. In Europe, the industry has sought to evade advertising restrictions by advertising Camel boots in Norway, Camel matches and Marlboro lighters in Belgium, and Marlboro leisure wear in Sweden.

**Health warnings:** In 1991, 77 countries required health warnings on cigarette packages, but in many countries the warning is weak and familiar, stating simply that smoking is dangerous to health. Forty countries require a statement of tar and nicotine contents and sometimes the carbon monoxide emission. India wisely requires warnings in both English and the Indian languages.

An important development has been recognition of the effectiveness of strong rotating warnings pioneered by Sweden (Table 1). Iceland made a further innovation when it added illustrations to the warnings (Fig. 1). Norway has adopted rotating warnings and is planning to add illustrations (Fig. 2). Other countries that have adopted rotating warnings are Canada, Finland, Ireland, the United Kingdom and the USA.

Only rarely does a warning inform the consumer that tobacco is addictive, which explains why it is so difficult to quit. One warning for snuff and chewing tobacco in Sweden, however, states that these products contain nicotine and they may therefore, be as addictive as tobacco.

Concerning snuff and smokeless tobacco, five countries have banned the importation and sale of moist snuff and smokeless tobacco — Hong Kong, Ireland, Israel, New Zealand and the United Kingdom. This ruling is important in countries where this product has not taken hold, and its dangers are not known.

Table 1

*New rotating health warnings on cigarettes in Sweden*

- 
- Do not expose your colleagues to tobacco smoke. It is harmful and irritating. National Board of Health and Welfare
  - Tobacco smoke contains many carcinogens. The smoke in passive smoking, which affects those in the vicinity of the smoker, contains the highest level of carcinogens. National Board of Health and Welfare
  - Tobacco smoking lowers resistance to infections, including those of the respiratory tract. National Board of Health and Welfare
  - Do not smoke when children are present. Smoke irritates their respiratory tract. National Board of Health and Welfare
  - If you are pregnant or breast-feeding, do not smoke; both you and your child may be harmed. National Board of Health and Welfare
  - In 1983, 779 persons died in traffic accidents and at least 8000 from tobacco smoking. National Board of Health and Welfare
  - Lung cancer among women will soon be commoner than breast cancer. Smoking is the cause. National Board of Health and Welfare
  - Almost all persons suffering from arteriosclerosis affecting the blood vessels of the legs and having difficulty in walking are smokers. National Board of Health and Welfare
  - It is practically only smokers who have a heart attack before they are 50. National Board of Health and Welfare
  - Smoking heightens the risk of inflammation of the gums. This can lead to loss of teeth. National Board of Health and Welfare
  - If one person smokes, everyone smokes. Most tobacco smoke enters the air breathed by everyone. Your smoking may harm others. National Board of Health and Welfare
  - The combination of smoking and contraceptive pills heightens the risk of a heart attack for women over 30. National Board of Health and Welfare
- 

But in India, where tobacco is chewed as an ingredient of betel quid; mixed with lime and areca nut; and is applied in the form of *mishri*, snuff and tobacco toothpaste (see paper by Bhonsle *et al.*, this volume), the problem is



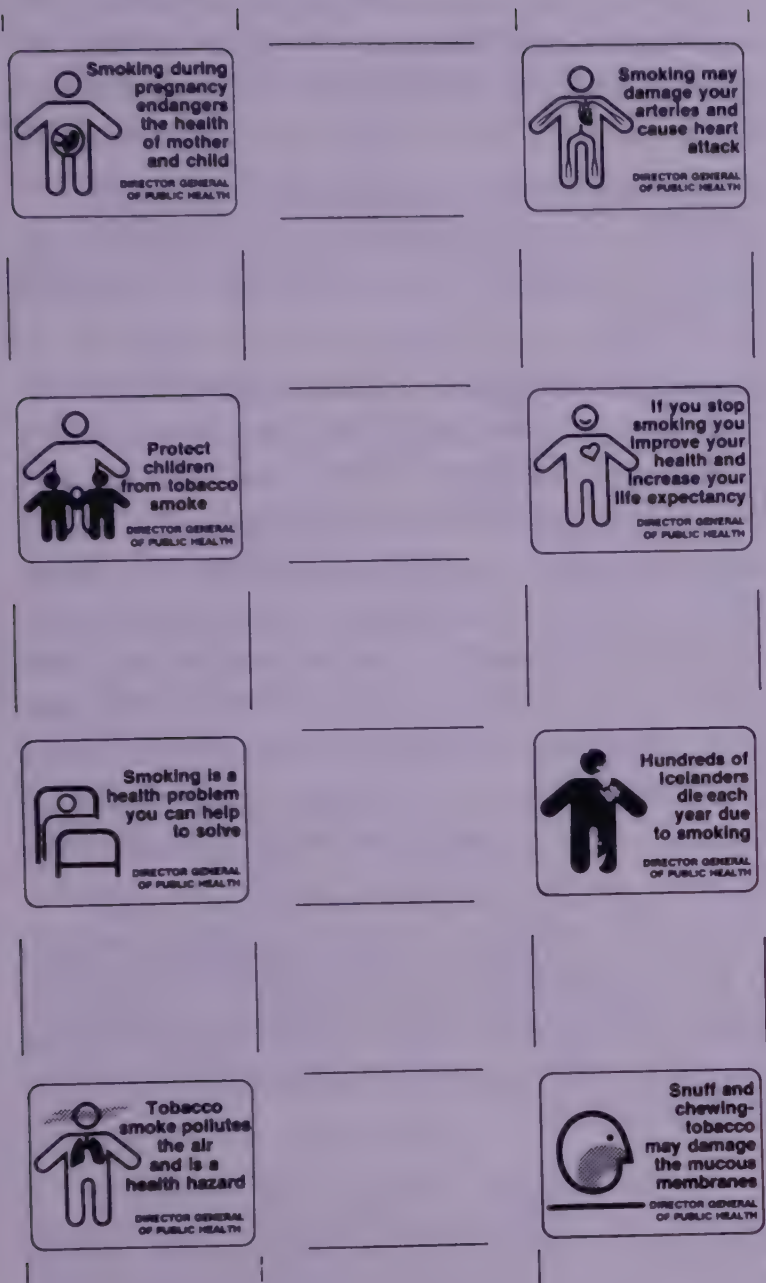


Fig. 1. Icelandic health warnings on tobacco products

more difficult. Many of these traditional forms of tobacco use have been shown to be associated with oral cancer and precancerous lesions (see paper by Murti *et al.*, this volume) and excess mortality (14).

**Control of harmful substances:** Twenty-six countries set maximum levels of tar and nicotine in cigarettes. This fact is an important issue in developing countries, because the multinational companies market cigarettes with much higher levels of tar and nicotine in the developing countries as compared to the same brands in industrialized countries. Cigarettes manufactured in the Philippines were found to

be almost twice as harmful as the same brands manufactured in the USA (15).

Although there is some difference of opinion on whether low-tar, low-nicotine cigarettes provide any protection for the smoker, British authorities attribute some of the reduction in British cancer mortality to low-tar cigarettes (16). Nigel Gray of Australia favours reducing the tar content of cigarettes to 5-15 mg through one of three strategies — legislation, voluntary agreements with the industry or increasing the tax on high-tar cigarettes (17). Legislation has the advantage of permitting progressive reduction in tar levels.

**Restrictions on sales to adults:** Restrictions on places where cigarettes may be sold

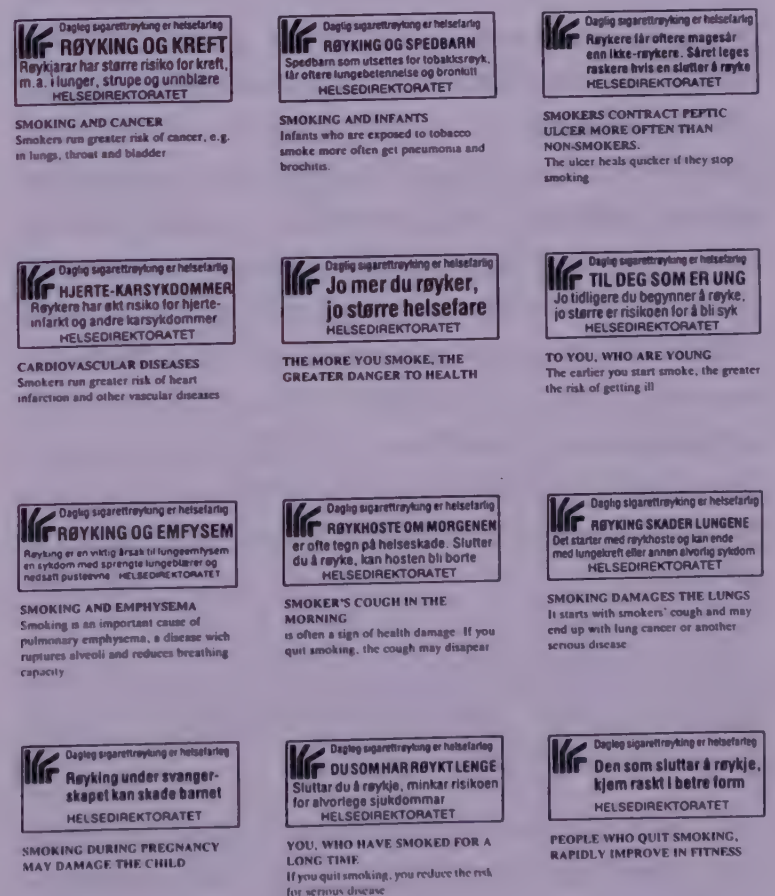


Fig. 2. Norwegian health warnings on tobacco packages. Each brand has to carry these warnings, equally distributed, on packets that are sent out on the market. All the warnings are signed by the Directorate of Health, and have a common introduction: 'Daily cigarette smoking is dangerous to health'.



contribute to the creation of a smoke-free environment. The most common type prohibits sales in health institutions and government buildings (see paper by Joseph, this volume). Many institutions restrict such sales voluntarily. This type of legislation is viewed as relatively weak; much stronger action consists of banning not only sales, but all smoking in health and educational institutions.

**Tax and price policy:** Increasingly, tax and price policy is being recognized as a powerful weapon to reduce tobacco use, especially among young people. It has been demonstrated both theoretically and in practice that increasing taxes and prices of cigarettes lowers consumption because the demand for tobacco is elastic and responds to changes in price (18-20).

The importance of price policy in decreasing consumption was shown in Finland, which, despite its strong antitobacco legislation, had not succeeded in reducing consumption of tobacco and mortality among adult men. Investigation revealed that, unless the price of tobacco keeps pace with inflation and takes into account increases in real income, there will be little or no decline in smoking because tobacco will be a cheap luxury. A governmental commission in Finland recommended regular, substantial price increases — as much as 17% in a single year, stating: "Every tobacco price decision is also a health policy decision: a decision as to the amount of tobacco-related illness and premature deaths in the future" (21).

In a number of countries, higher taxation has raised the cost of cigarettes substantially. In Norway, taxes on cigarettes have been raised 20-25% since 1975 and now account for 65% of cigarette prices. In the State of California, voters passed a 25-cent increase in the tax on each package of cigarettes, yielding US\$ 600 million in the first year for health education on tobacco and for other health and educational purposes.

Two types of tax and price increases have been levied on tobacco: (i) general tax increases; and (ii) differential taxes imposing a supplementary tax on high-tar cigarettes. In some instances a certain percentage of the tobacco tax is earmarked to education on tobacco and health and other tobacco-control activities.

**Economic strategies:** Tobacco production has a number of advantages for governments (see papers by Sanghvi; Chari and Rao; and Luthra *et al.*, this volume). Tobacco is a remunerative crop; it provides employment; it raises revenue (5% of the Indian Government's revenue in 1975 came from taxes on tobacco); and it increases exports and provides hard currency. But there is also a downside to tobacco production. Tobacco requires investment of capital, use of warehouses, transport and technical expertise that could better be used for nutritious crops (4). Economic costs to society in lost productivity and health care expenditures are exceeded only by the human suffering caused by tobacco use (see paper by Luthra *et al.*, this volume).

Achieving the abolition of subsidies for tobacco production, substituting other crops, providing new rural employment, and developing alternative sources of government revenue are formidable tasks that will require great ingenuity and political will (see paper by Chari and Rao, this volume). No country has as yet undertaken a major programme of crop substitution. The state of Kerala in India has made a step in this direction by showing that tobacco can be rotated with rice (4).

## WHAT ARE THE FEATURES OF VARIOUS TYPES OF LEGISLATION THAT INFLUENCE SMOKING PRACTICES?

**Restrictions on smoking in public places:** Mounting evidence on the dangers of passive smoking has led more countries to enact restrictions on smoking in public places and



has caused countries with legislation to expand the number of public places where smoking is prohibited. As of 1991, 90 countries had such legislation.

Of particular importance is the increase in the number of public places where smoking is prohibited. Finland has long banned smoking in all public places unless it is specifically allowed. Belgium has banned smoking in all indoor places to which the public is admitted. Norway has restricted smoking on premises and means of transport to which the public has access and in meeting rooms and work premises where two or more people meet. The USA has banned smoking on virtually all domestic commercial airline flights. 'The New York City Clean Indoor Air Act' prohibits smoking in all enclosed areas within public places when the public is invited or permitted.

Equally noteworthy is the fact that these broad statutes have been readily accepted by the people. Opposition to implementation has been minimal, and, where it existed, it has been easily overcome by education and public support for the restrictions.

Restaurants present a special problem, and the solution generally has been to require nonsmoking sections in restaurants with more than a certain capacity.

**Restrictions on smoking at the work place:** Restrictions on smoking in the workplace are closely linked to control of smoking in public places, since many of the public places where smoking is restricted are also workplaces. Passive smoking is more harmful, of course, in a place where a worker spends a whole day than in a meeting room or cinema where a person stays for a couple of hours. Smoking is particularly dangerous in factories and mines, where it accentuates the effects of toxic materials.

National legislation to control smoking in the workplace exists in about 12 European countries. In the USA, numerous city and

county ordinances have been enacted to protect nonsmokers in the workplace. These ordinances, which tend to cover principally white-collar workers, provide for accommodating the interests of smokers and nonsmokers. Where they cannot be accommodated, the issue must be resolved in favour of nonsmokers.

**Preventing young people from smoking:** The importance of taking every measure that will prevent tobacco use by young people cannot be overestimated. On 'World No-Tobacco Day' in May 1989 in Geneva, Richard Peto, co-editor of the 1986 report from the International Agency for Research on Cancer, 'Tobacco — A Major International Health Hazard', gave the following chilling information about China: "Among people who smoke manufactured cigarettes regularly throughout adult life, about one in four will be killed by tobacco. Thus, of the young people aged under 20 now living in China, about 50 000 will eventually be killed by cigarettes. Many others will be disabled by chronic shortness of breath. Because of recent increases in cigarette manufacture, the number of deaths from tobacco in China will rise over the next few decades from about 100 000 a year now to about 2 000 000 a year in 2025, when today's young people are middle-aged". (22) It has been shown in India that at least 630 000 deaths annually are attributable to tobacco (14).

What, then, can we do to prevent young people from starting to smoke and stop them from continuing to smoke? A number of legislative measures target young people. These include: (i) prohibiting sales of tobacco to minors and enforcing the prohibition, (ii) prohibiting sales from vending machines, (iii) prohibiting sales of single cigarettes, (iv) prohibiting free distribution of cigarettes, (v) prohibiting sales and smoking in schools and other places frequented by young people, (vi) restricting advertising that influences young people, (vii) banning sales of snuff and smokeless tobacco, and (viii) mandating effective education on the dangers of tobacco.



In addition to these measures aimed specifically at young people are all the strategies directed at the population as a whole that also influence young people. These include: (i) prohibiting all direct advertising and indirect sponsorship of tobacco, (ii) decreasing the tar content of cigarettes, (iii) mandating powerful health warnings, and (iv) increasing the tax on cigarettes.

**Mandating health education:** While effective health education may exist in the absence of legislation, mandating health education on tobacco is powerful because it expresses governmental policy, promotes universal implementation of the requirement, and may allocate financial resources from governmental revenues or tobacco taxes.

### HOW IS LEGISLATION IMPLEMENTED?

Several strategies assist the implementation of legislation. Most important is public education about the law before, during and after its enactment. Communication of such information to the people enlists their support and cooperation in implementing, for example, legislation to control smoking in public places.

Another approach is to develop regulations setting forth and publicizing the steps or phases by which a law will be implemented. Norway has used this approach in implementing its law on control of smoking in public places.

To enforce a ban on sales to minors, the imposition of a well-publicized fine on a violator sends a strong signal to all vendors of tobacco products. Statutes may require posted signs that tobacco sales to minors are illegal, may require purchasers to show proof of age, may require licensing of sellers of tobacco, and may increase the penalties for violation of the law.

### WHAT IS THE EVIDENCE THAT LEGISLATION IS EFFECTIVE?

It is difficult to evaluate the effects of specific types of legislation because so many factors

are involved in tobacco use, but evidence is increasing that specific interventions are effective. Warner demonstrated that smoking declined in association with a requirement for showing antismoking messages on television (23).

The decline in smoking associated with price increases has been shown in Hong Kong (24), the Netherlands (25), the United Kingdom and the USA (13). A Swedish investigation showed the positive impact of rotating warnings in diminishing consumption of cigarettes (13).

Tye *et al.* (26) showed that advertising increases consumption and that the industry's contention that advertising is designed only to influence brand share of the market is specious, since cigarettes enjoy one of the most tenacious brand-loyalties of any consumer product.

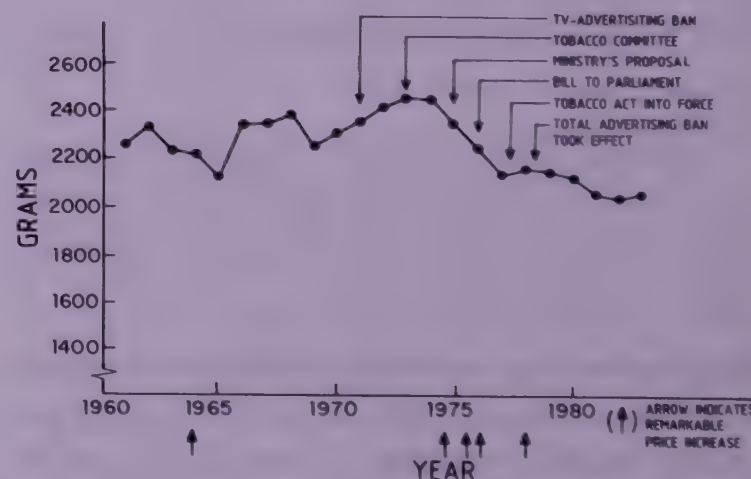


Fig. 3. Total consumption of tobacco products per adult population and some antismoking measures in Finland; moving averages of three years. (Source: The National Board of Health, Finland)

Figure 3 shows the relation of legislation to consumption of tobacco in Finland as the restrictions took effect, and Figure 4 shows the experience in Norway as the Norwegian government moved to enforce its legislation and



imposed successive price increases. In Iceland, where a comprehensive antitobacco law took effect in 1985, there was a decline in daily smoking adults one year after the law took effect (Table 2).

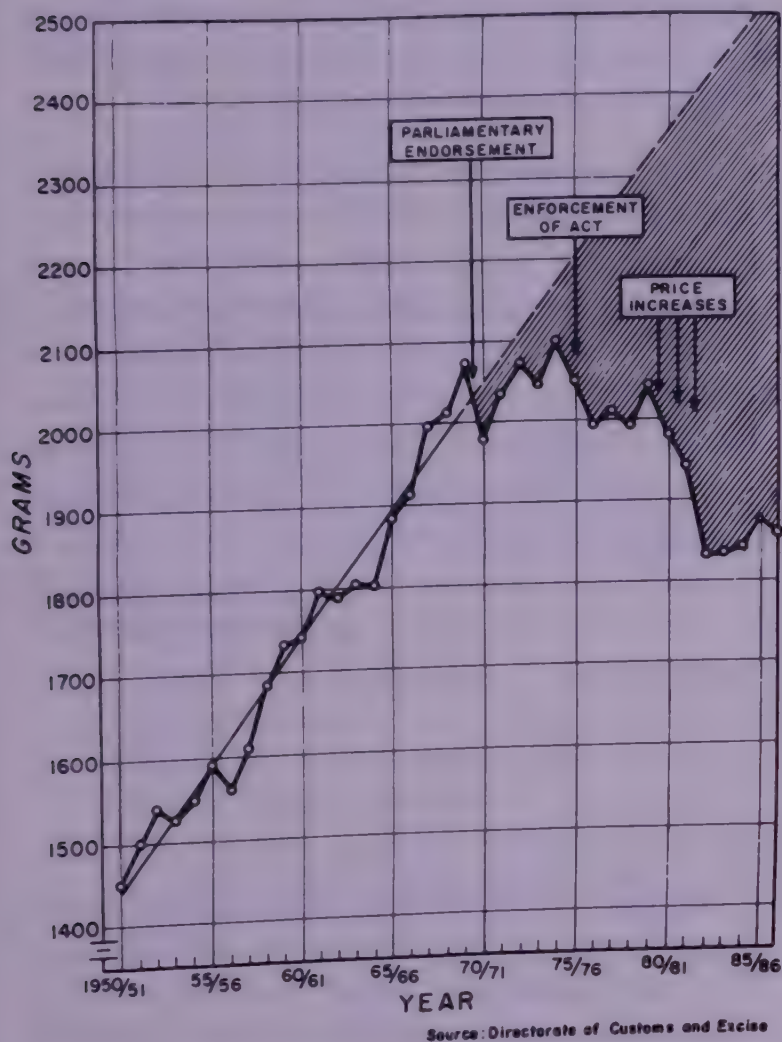


Fig. 4. Per-caput consumption (aged  $\geq 15$ ) of cigarettes and smoking tobacco in Norway with time.

Table 2

*Daily smoking among 18 to 69-year-olds in Iceland<sup>a</sup>*

	1985		1986	
	%	Size of the sample	%	Size of the sample
Men	42.9	1356	37.2	1167
Women	37.0	1352	35.2	1121
Total		2708		2288

<sup>a</sup>Source: Icelandic Smoking Control Programme (Directorate of Customs and Excise)

## WHAT ARE THE PRIORITIES IN LEGISLATION?

Each country must, of course, decide the priorities that best fit its needs: needs may be quite different in a huge country like India, with a large, diverse rural population, from those in small countries with homogeneous populations. These differences affect the form that legislation takes; but, on the basis of experience, we may agree on certain priorities: (i) banning all tobacco advertising, promotion of a tobacco free society, and reducing pressure on young people to smoke; (ii) regular and substantial increases in taxes and prices that decrease the demand for tobacco, especially among young people; (iii) restricting smoking in public places and the workplace makes a strong statement that smoking is socially unacceptable (It is generally agreed that social acceptability is the ground on which the battle against tobacco will be won or lost); and (iv) clear antismoking messages, delivered to children and young people in schools and to the people as a whole, are an essential component of an effective programme.

## WHAT OVERALL STRATEGIES ASSIST THE DEVELOPMENT OF A SOUND PUBLIC POLICY ON TOBACCO?

A key factor in the progress that has been made in combatting the smoking epidemic has been the development of antitobacco networks, consisting of governmental and voluntary organizations, health professionals, and consumers.

At the international level, the WHO has taken the lead. Non-governmental international organizations, particularly the International Union Against Cancer (UICC), have been strong allies. WHO has reached out to other organizations in the United Nations system, with differing responses.

In recent years, initiatives at the regional level have been accelerated. In 1988, the European Regional Office of WHO and the



Europe against Cancer Programme of the European Community held a conference in Madrid to energize the European countries. In 1989, the International Union for Circumpolar Health, the Danish Cancer Society and the European Office of WHO held a meeting in Yellowknife, Northwest Territories, Canada to address the high rates of tobacco-related disease among the indigenous peoples of the nations bordering the North Pole.

At the national level, most countries have found it important to establish a central body to develop and coordinate activities on control of tobacco use. Such a body may be either a governmental organization or a voluntary organization, supported in part by governmental funds. Such a central focal point provides high visibility for antitobacco efforts.

Within countries, professional and voluntary agencies have important contributions to

make in providing health education, in undertaking cessation activities and in organizing communities to support antitobacco programmes, not the least of which is consumer advocacy for a smoke-free society. Non-smokers' rights organizations can mobilize citizens and provide a consumer voice loud enough to persuade politicians to act.

In conclusion, it is reiterated that legislation is a powerful tool for developing and implementing sound public policy on control of tobacco use. It can bring forth the benefits of scientific knowledge to protect the health of the people and can create leverage for health promotion. Furthermore, it can serve as a basis for imaginative programmes to control smoking. Legislative action is essential, in fact urgent, if the worldwide assault of the tobacco industry on the people's health is to be effectively combatted.

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# Controlling cancer by suing tobacco companies: the potential for India in the light of the US experience

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Litigation on the liability presented by tobacco products is now widely recognized as providing unique opportunities for discouraging tobacco use by raising product prices and focusing public attention both on the misleading nature of tobacco promotions and the actual dangers of using the products. In view of the recent legal precedents from suits on motor accidents and the Bhopal gas tragedy, India has potentially the most promising legal environment for bringing such litigation.

## INTRODUCTION

Lawsuits against tobacco companies are potentially powerful tools for controlling tobacco consumption. They have also proven — like most other such tools — to be difficult to wield and slow to produce results. Recent legal developments have made these cases easier to bring and more likely to win in the USA; Indian legal developments also suggest that such lawsuits, perhaps in a slightly different legal form, might also succeed.

## POTENTIAL BENEFITS

The benefits sought from litigation on tobacco product liability include: (i) forcing the manufacturers to raise the price of tobacco products (to cover the expected cost of litigation and judgment), thus discouraging consumption; (ii) forcing the manufacturers to stop lying about the dangers of their products and, indeed, to 'volunteer' the truth about them; (iii) discrediting the industry in the legislative arena by releasing internal documents giving details of their disinformation campaign and their disregard of public health; and (iv) publicizing the dangers of tobacco use through

media publicity attendant upon the filing and trial of such suits.

## THE US EXPERIENCE

Difficulties that have arisen in bringing these suits in the USA include: (i) the willingness of the tobacco industry to spend endless amounts of money to intimidate plaintiffs and delay proceedings; (ii) the ability of the industry to evoke 'blame-the-victim' attitudes among judges and jurors by exaggerating the extent of both past and current public awareness of the dangers of tobacco use and by presenting a misleading picture of the amount of individual choice involved in the continued use of tobacco products; (iii) adverse judicial decisions resulting from judges' fears of a flood of litigation if the suits are permitted to proceed; and (iv) poor choice of plaintiffs in the first suits (weak etiological evidence and no effort to quit even after warnings received).

Recent, positive US legal developments have made each of these difficulties much less formidable. First, evidence about the knowledge and behaviour of the multinational tobacco companies, developed by plaintiffs and



lawyers at great expense for use in their trials, is now available cheaply from the Tobacco Products Liability Project. Also, five years of experience in fighting the tobacco companies have prepared the plaintiffs' bar for dealing effectively with the defendants' arguments and litigative devices. Cases against tobacco companies are now no more expensive to bring than other complex product liability cases.

Second, the decision on 5 January 1990 of the US Court of Appeals in *Cipollone vs. Liggett Group, Inc.* makes clear that juries will have to compare knowledge of the dangers of tobacco held by tobacco companies and by individual consumers at specific times in the past, rather than anachronistically evaluating earlier behaviour in the light of current levels of public knowledge. Furthermore, the 1988 US Surgeon-General's Report on Nicotine Addiction has helped change public consciousness on the amount of choice exercised by most long-time smokers.

Third, the fact that the first plaintiff's verdict in June 1988 in the *Cipollone* case did not lead to a flood of new cases has encouraged courts to begin decide tobacco-related cases consistently with the way they treat those on manufacturers of other dangerous products. Thus, the 5 January 1990 appellate decision in *Cipollone*, 'although it reversed the US\$ 400 000 verdict and remanded the case for a new trial, for the first time allowed the plaintiff to use a risk-benefit analysis, which holds manufacturers liable whenever the risks of their products to consumers exceed the benefits. This holding, along with the court's strengthening of the 'failure-to-warn' and express warranty theories of action, opens up powerful legal theories for plaintiffs' attorneys.

Finally, plaintiffs' attorneys have learnt which cases to avoid.

The benefits achieved from tobacco litigation in the USA to date include: (i) at least a

modest contribution to both snuff and cigarette price increases (which the industry explained were needed, in part, to cover litigation expenses); (ii) forcing the industry to adopt a defensive public relations posture of 'if you die from smoking, it was your own choice' — hardly the best way to sell cigarettes; (iii) releasing damaging internal documents which discredited the industry politically; and (iv) focusing public attention not just on statistics, but on the fact that real individuals die from tobacco use.

## THE INDIAN POTENTIAL

The Indian legal situation is quite different from that of the USA, yet it appears to hold substantial possibilities for producing similar public health benefits from tobacco litigation. While product liability actions — and tort claims in general — have traditionally been rare, three recent legal developments in India have made it a potentially hospitable environment for litigation against multinational tobacco companies.

First, in two 1987 cases, the Indian Supreme Court articulated tort principles that were more liberal even than the risk-benefit test enunciated in the *Cipollone* case. Thus, in *Gujarat State Road Transport Corporation vs. Ramanbhai Prabhatbhai*, the court held for the first time that 'liability without fault' was 'a principle of social justice' in automobile accident cases. Then, in *M.C. Mehta vs. Union of India*, involving a pre-Bhopal release of toxic gases from a factory, the court articulated its willingness to go beyond the principles of liability applied in the United Kingdom and other foreign countries, and it illustrated this willingness by holding that: "If the enterprise is permitted to carry on a hazardous or inherently dangerous activity for its profit, the law must presume that such permission is conditional on the enterprise absorbing the cost of any accident arising on account of such hazardous or inherently dangerous activity, as an appropriate item of its overhead.



While the immediate application of this principle was to an industrial accident, the principle itself and the underlying reasoning were broad enough to encompass tobacco liability cases.

Particularly encouraging for our purposes is the paragraph of the Mehta opinion immediately following this discussion:

"We would also like to point out that the measure of compensation in the kind of cases referred to in the preceding paragraph must be correlated to the magnitude and capacity of the enterprise because such compensation must have a deterrent effect. The larger and more prosperous the enterprise, greater must be the amount of compensation payable by it for the harm caused on account of an accident in the carrying on of the hazardous or inherently dangerous activity by the enterprise."

Philip Morris and British American Tobacco are both very large and very prosperous!

Second, while India does not permit contingency fees (which, in the USA, recruit plaintiffs' attorneys by offering them part of the eventual recovery), the Indian Supreme Court has in recent years recognized a category of 'public interest litigation' in which it is

willing to order defendants to compensate public interest plaintiffs for their expenses. This action, along with court rules which permit class actions, could facilitate injunctive actions against abusive industry practices, as well as perhaps carefully planned and respectably sponsored test cases in the product liability arena.

Finally, the political and legal ferment around the Bhopal disaster, focusing on the role of tort law both in deterring multinational corporations from dangerous practices and in providing compensation to large numbers of victims, appears to have produced a new receptivity among Indian judges, lawyers and politicians to the need for effective legal remedies for tortious acts injuring large numbers of people. I assume that in India, unlike the USA, the tobacco industry could not plausibly claim that everybody who uses tobacco products should know (and should have known for many years) of the attendant dangers; on the other hand, there is abundant evidence that Philip Morris and British American Tobacco should have known of these dangers for several decades. In this context, a public advocacy of tobacco product liability suits by respected Indian public health authorities could produce a positive public and judicial response.





# Antitobacco campaign in Maharashtra, India: achievements and perspectives

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Recognizing that cancer is a preventable disease, the Government of Maharashtra, India, undertook an aggressive antitobacco campaign, consisting of health education programmes, slogans and billboards reminding nonusers of their right to a tobacco-free environment; a counter-campaign against cigarette advertisements was launched in Bombay City. Coupled with these activities, legislation was enacted making smoking in Government establishments and closed spaces in Maharashtra an offense.

## INTRODUCTION

Most public health programmes of the Government of India are directed to communicable diseases such as malaria, tuberculosis and leprosy. The occurrence of certain diseases due to life style has now been recognized, and public health programmes are also being mounted against them. Lung cancer is one fatal but preventable life-style disease. The Government of the State of Maharashtra, India, thus initiated a campaign against smoking in 1986. The first reaction of smokers, mostly from urban upper-middle classes, was "We smoke because we like it. It is none of your concern. After all, it is we who would suffer, not you".

After experience of rejoinders of that type, an aggressive antitobacco campaign was launched in Maharashtra. This paper summarizes those activities and gives details of the legislation enacted against tobacco.

## ANTITOBACCO MEASURES

**Awareness of passive smoking:** To counter indifferent attitudes of the kind illustrated above, the Public Health Department of the Government of Maharashtra adopted the

slogan 'Your smoking is injurious to our health'. To support this line, a poster was designed depicting a half-smoked cigarette, with a man at one end and his wife and young daughter at the other end, coughing. This poster, which was displayed on the sides of buses, led to awareness of the hazards of sidestream smoke and of passive smoking. It was assumed that realization of the fact that smoking might be harmful to others in a family would at least incite people to keep away from children while smoking. Interestingly, non-smokers began to use this slogan to counter the indifference of smokers. Youngsters reading this slogan aloud gave a clear but polite signal to nearby smokers either not to smoke or to move away. It also served to counter the rude antagonism of smokers towards antismoking activities.

In January 1987, the Tata Memorial Hospital, Bombay, and the Public Health Department of the Government of Maharashtra organized a two-day workshop on cancer in collaboration with the UICC, where a plan for a State cancer control programme was adopted. One of the strategies was to launch an aggressive anti-tobacco campaign. Perhaps



the only action that had been taken against tobacco use up to that time had been national legislation in 1975 that all cigarette packets and cigarette advertisements display a warning to the effect that 'Cigarette smoking is injurious to health'. Most manufacturers and advertisers ran the sentence, but preceded it with the words 'statutory warning'.

**Smoking as a criminal offense:** A move was made to make smoking in Maharashtra Government offices an offense. A proposal was initiated by the Public Health Department that resulted in billboards being put up in the corridors of the State Secretariat to the effect that 'Smoking is prohibited'. Predictably, however, this measure did not prove to be effective, indicating that an administrative order alone would be of no great value. A more powerful means of curbing smoking was found in certain provisions of the 'Bombay Police Act 1951', which read as follows: "Section 116: No person shall in any court, police station, police office, building occupied by Government or building occupied by any public body, smoke or spit in contravention of a notice by a competent authority in-charge of such places and affixed to such court, station, office or building. Section 117: Any person contravening the provisions of section 99 to 166 (both inclusive) on conviction, be punishable by fine which may extend to Rs. 100/-."

These provisions were explored to make smoking and spitting within Government offices a criminal offense. Applications were made to the Home Department and to the General Administration Department of the Government of Maharashtra. Finally, approval by the Minister of State for Health and the Health Minister was obtained, and orders were issued on 5 August 1987. A copy of the order is reproduced as Appendix.

The prohibition applies not only in built-up areas but the premises, including compounds. (i) The notice-boards, the colour scheme and the material to be displayed were

specified; since these boards were put up right outside the gate, the campaign drew special attention. (ii) An antismoking environment was created by removing ashtrays from all Government offices in Maharashtra. (iii) Even cigarette and *bidi* kiosks within the premises of Government offices were closed down.

Within two days after these orders were issued, a small news item appeared opposing them. 'The workers in *bidi*-making units would march to the secretariat to protest', the news item stated. The march did not materialize; on the contrary, newspapers reported readers' satisfaction about the Governmental action. One letter read, "Why is it that Maharashtra Government is selfish? Why do they take care of their own employees? What about banning smoking in public spaces?"

**Health education:** Smoking can perhaps be prevented in Government offices by means of a Government order, but an intensive public education campaign is required to prevent people from smoking in public places. It was felt that, with a proper approach, such a campaign would incite a groundswell demanding legislation to restrict tobacco use, sales, advertisement and even cultivation.

'Wills' is a popular brand of cigarette manufactured by a leading firm, the Indian Tobacco Company, a subsidiary of British-American Tobacco. They advertise their product with attractive models and the slogan 'Made for each other', stating that the filter and tobacco are well matched. The anti-smoking advertisement used the same format but changed the content to imply that smoking and cancer are made for each other. A huge hoarding was erected at one of the busiest traffic roundabouts in Bombay (at Haji Ali) on the night of 31 December 1987, as a New Year's gift to the citizens of Bombay!

The Indian Tobacco Company, which was in the process of putting up its usual hoardings for 'Wills' in the same area, stopped the painting midway. Instead it put up the



hoarding of another of its brands, 'Bristol,' with the message 'I get what I want'. This was counteracted with an anti-advertisement slogan 'I get what I do not want — cancer'. Another manufacturer uses the slogan 'Taste the spirit of freedom'. To neutralize this, the visual content of the advertisement was changed to vultures and the caption to 'Taste the spirit of free doom'.

Several other slogans and hoardings were designed for the antismoking campaign. In an attempt to enlist the support and services of the women, one hoarding had 'Smoker stinks. Cigarette harms' on one side, and 'Be wise, live longer, choose a nonsmoker' on the other.

## **DISCUSSION**

Maharashtra State is proud of its aggressive, blunt, outspoken and innovative antitobacco

campaign. It has banned smoking and spitting in Government offices and made these acts a criminal offense. The orders are generally implemented properly, and many senior officers in Government departments in Bombay have stopped smoking in their offices. The penalty on conviction is a fine of only Rs. 100/- (US\$ about 5); but the issue is one of criminal conviction. There may be a few violations, but the measure has created a fear of being convicted and a feeling of guilt about breaking the law. Furthermore, the environment for giving up tobacco use has become more congenial. We believe that this approach, with new slogans, new programmes and an aggressive antitobacco counter-campaign, has resulted in the creation of greater awareness of the harmful effects of tobacco and nonsmokers' right to have a tobacco-free environment. It is gratifying to note that other states in the country are undertaking similar measures.

## Appendix

Cancer Control Programme Ban on smoking and spitting in Government/Semi-Government offices and institutions

GOVERNMENT OF MAHARASHTRA  
Public Health Department  
Resolution No. CNC 1086/CR 241/PH-6  
Mantralaya, Bombay 400 032, dated 5 August, 1987

According to the estimates made by experts, there are 1.5 million cancer patients in the country at present. It is also estimated that 0.5 million new patients are added every year. Taking into consideration the increased longevity of the citizens in the country and at this rate, the number of cancer patients by 2000 AD is likely to have been tripled. According to the observations of the Indian Council of Medical Research, out of the total number of cancer patients, cancer could be prevented in respect of 40% totally. In respect of 30% cancer patients it can be cured if it is detected in early stages. For remaining 30% cancer patients, only long-term treatment/therapy can be given. Taking this position into consideration, the importance of preventive measures in Cancer Control Programme is self evident.

Among cancer patients, the number of patients, who are affected by cancer due to tobacco, is large. Smoking and tobacco-chewing not only cause cancer but also can cause respiratory and digestive system diseases. It is therefore necessary to prevent citizens from these diseases and to motivate them to refrain from smoking and tobacco-chewing. Government has, therefore, as an important preventive measure, decided to ban smoking and spitting in Government, Semi-Government, Zilla Parishads, Municipal Corporations, Municipal Council Offices and Institutions and Undertakings coming within the purview of the State Government.

2. Bombay Police Act 1951 has the following provisions:

**Section 116:** No person shall, in any Court, Police Station, Police Office, Building occupied by the Government or by any public body, smoke or spit in contravention of a notice by a competent authority in-charge of such places and affixed to such Court, Station, Office or Building.

**Section 117:** Any person contravening the provisions of Section 99 to 116 (both inclusive) on conviction, be punishable by fine which may extend to Rs. 100/-.

3. Government directs that competent authorities in all Government, Semi-Government offices, Zilla Parishad, Municipal Council, Municipal Corporation Offices and Institutions, and Undertakings shall take recourse to the above provisions of Bombay Police Act, 1951 and should ban smoking and spitting. While implementing this, the accompanying guidelines should be followed. These orders shall come into effect immediately.

All Mantralaya Departments should instruct the Heads of Offices and Government Undertakings under their control to follow these orders.

By order and in the name of the Government of Maharashtra.

Sd/-  
Arun Ghate  
Section Officer



Accompaniment to Government Resolution, Public Health Department, No. CNC 1086/CR 241/PH-6, dated 5 August 1987.

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*Guidelines for ban on smoking and spitting*

- (1) In every room of the office or institution a Board having the following words may be displayed. *Smoking strictly prohibited* (Punishable under Section 116 and 117 of Bombay Police Act 1951). The size of the board should not be less than 15 x 45 cm.
- (2) Similar boards should be displayed on the wall outside every room of the institution or office, if there is ample vacant space available, for example, Corridor, Out-patient Department, Meeting Hall. Such boards in Marathi and English as above should be displayed at a distance of every three metres.
- (3) At every entrance of the building, a board of the minimum size of 60 cm x 75 cm should be displayed and the following words should be displayed in Marathi and English. *Smoking and Spitting strictly prohibited inside this building and compound.*
- (4) A similar board of minimum size of 90 cm x 60 cm should be displayed at the entrance of the compound of the building.
- (5) All these boards should be of permanent nature i.e. wooden, tin or of similar material. The ground colour of the board should be red and the words in white. If some period is likely to be taken for preparation of the permanent boards, temporarily, paper or card board boards should be displayed.
- (6) The boards on the wall should be at a minimum height of 1.5 metre.
- (7) If any ash-trays have been kept in any of the rooms or elsewhere in the institution or the office, they should be removed.
- (8) If there are any *pan-bidi* vendors in the building or in the compound of the building, they should be moved outside the compound of the building.

The first of these is the fact that the system is not a simple one, but a complex one, involving many different factors and many different people.

The second is the fact that the system is not a static one, but a dynamic one, which is constantly changing and evolving.

The third is the fact that the system is not a closed one, but an open one, which is constantly interacting with the outside world.

The fourth is the fact that the system is not a homogeneous one, but a heterogeneous one, which is made up of many different parts and many different people.

The fifth is the fact that the system is not a linear one, but a non-linear one, which is characterized by many different feedback loops and many different interactions.

The sixth is the fact that the system is not a deterministic one, but a probabilistic one, which is characterized by many different uncertainties and many different risks.

The seventh is the fact that the system is not a simple one, but a complex one, involving many different factors and many different people.

The eighth is the fact that the system is not a static one, but a dynamic one, which is constantly changing and evolving.

The ninth is the fact that the system is not a closed one, but an open one, which is constantly interacting with the outside world.



# **CONSENSUS SUMMARY AND RECOMMENDATIONS**





## Consensus summary and recommendations

### SUMMARY OF PRESENTATIONS

Tobacco is chewed, smoked and applied on the oral mucosa in a variety of ways all over the world, and a large spectrum of tobacco products is manufactured and marketed for human consumption. Wherever research has been done, the use of tobacco in any form has been found to damage health seriously. Any manufactured item containing tobacco and used following the manufacturers' instructions or intention will cause a significantly high risk of ill-health. Inclusion of tobacco in any product meant for human consumption is unacceptable.

The best known and commonest tobacco product all over the world is the cigarette. The health consequences of cigarette smoking, such as lung and other cancers, heart disease, respiratory disease and pregnancy outcome, have been documented beyond any reasonable doubt. All over the world, tobacco-related cancers are a major public health problem and constitute one, two or three of the leading cancer sites out of the first five. Cigarette smoke may also cause lung cancer among nonsmokers, and children exposed to cigarette smoke may suffer from serious respiratory illness. Many studies document the extreme danger of all forms of tobacco use, including *bidi* smoking, chewing tobacco in any combination and reverse smoking, habits prevalent in India. For example, a *bidi*, which contains one-fourth or less of the tobacco in a cigarette, may deliver as much or more tar and nicotine. Certain forms of chewing tobacco have been demonstrated to contain high levels of carcinogenic tobacco-specific nitrosamines. In India, four of the five leading cancers are tobacco related.

Tobacco is a legal agricultural product, and products containing tobacco are legal all over the world. This situation, however, reflects a historical development rather than a desirable state of affairs. If tobacco or any product containing tobacco were to be introduced today, it would not meet existing health and safety standards anywhere in the world and therefore would not be marketed.

Tobacco has been identified as the largest single preventable cause of death and disease in the world today. It is estimated that tobacco causes 2.5 million premature deaths every year in the world. In India, tobacco is estimated to cause 630 000 premature deaths every year. In the interests of the health of the people, there is an urgent need to undertake specific measures to discourage the use of tobacco and its products.

### RECOMMENDATIONS

- \* Long-term goal: to create a tobacco-free society
- \* Short-term goal: to create an atmosphere in which the use of tobacco in any form, or the use of any tobacco product, is socially unacceptable rather than the norm.

#### The objectives of a tobacco control programme are:

- to reduce and stop the use of tobacco among those people who are already addicted to it; and
- to motivate nonusers of tobacco (especially the young), not to commence tobacco use.



**To achieve these objectives, two strategies are recommended:**

- (1) public education for a tobacco-free society; and
- (2) legislation and regulation to control the tobacco epidemic.

**RECOMMENDATIONS FOR IMPLEMENTING EACH STRATEGY ARE AS FOLLOWS:**

**Public education**

- A. Highest priority should be assigned to educating children and youth not to start tobacco use.
- B. Information on the ill-effects of tobacco use should be a prominent part of overall health education in the mass media.
- C. During the education of members of the medical community, i.e., medical and dental practitioners, nurses and paramedics, special emphasis should be laid on the adverse health effects of tobacco use. Instructions on preventing tobacco use and on cessation should be part of their professional curriculum.
- D. During their day-to-day work, medical personnel should pass on information on the hazards of tobacco use and how to prevent them.

**Legislation and regulation**

**A. Advertisements**

(i) Long-term strategy:

- Complete ban on advertisement of any product containing tobacco in any form. Advertisements of any item that has the same or a similar name as a tobacco product must also be banned.

(ii) Short-term strategy:

- Complete ban on advertising of tobacco in any audiovisual medium, including short advertisements in cinemas and in electronic media such as video cassettes;
- Complete ban on use of any pictorial or graphic display of any tobacco product in advertisements in print media; a ban on tobacco advertisements in print media may not be feasible as a short-term strategy;
- Health warnings should occupy at least 20% of the top area of advertisements. They should be rotated periodically and must have a graphic display indicating danger, e.g., skull and bones; this measure is especially important for populations that are not highly literate, as in India;
- Complete ban on sponsoring by a tobacco company or advertisement of a tobacco product for any sports, cultural or other public function;
- Complete ban on advertisement of tobacco products at the point of sale; places where tobacco products are sold must exhibit an appropriate health warning with a graphic display.

**B. Promotion**

- (i) Complete ban on all promotional activities for any tobacco product, such as free distribution, mailings and discount offers;



(ii) Complete ban on sales of all forms of tobacco to children.

C. Separation of smokers from nonsmokers

(i) Long-term strategy:

— Complete ban on smoking in any public place

(ii) Short-term strategy:

— Complete ban on tobacco use in all health centres and health facilities, such as hospitals, nursing homes and dispensaries;

— Complete ban on tobacco use in educational institutions, including schools and colleges;

— Separation of smokers from nonsmokers in public areas, such as transport facilities and restaurants. Where separation is not possible, as in theatres and exhibitions, smoking should be completely banned.





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This book on the control of tobacco-related cancers and other diseases would be a valuable resource for readers interested in any aspect of tobacco and health, specifically for state-of-the-art reviews, original research papers, thought-provoking articles, and its coverage of off-beat topics.

#### **About the editors**

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